

UNIV. OF
TORONTO
LIBRARY



Presented to
The Library
of the
University of Toronto
by

Iowa State Library

1 BINDING LIST MAR 1 1928

P
Med.
A
M

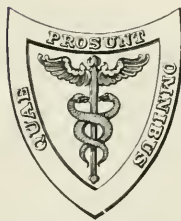
THE
AMERICAN JOURNAL
111

OF THE
MEDICAL SCIENCES

EDITED BY
GEORGE MORRIS PIERSOL, M.D.
JOHN H. MUSSER, JR., M.D.
ASSISTANT EDITOR

NEW SERIES

VOL. CLVI



222 471
3. 5. 28.

PHILADELPHIA AND NEW YORK
LEA & FEBIGER
1918

R
11
A5
m.s.
v.156
cop.2

COPYRIGHT
LEA & FEBIGER
1918

CONTENTS OF VOL. CLVI

ORIGINAL ARTICLES

The Ancient Factors in the Relations between the Blood Plasma and the Kidneys. By A. B. MACALLUM, M.D., F.R.S.	1
Typhoid Vaccine in a Case of Typhoid Spine. By W. ALLAN, M.D., and J. W. SQUIRES, M.D.	11
Electrocardiographic Evidence of Abnormal Ventricular Preponderance and of Auricular Hypertrophy. By PAUL D. WHITE, M.D., and ARLIE V. BOCK, M.D.	17
Cholesterohydrothorax. By B. F. WEEMS, JR., M.D.	20
The Chemotherapy of Leprosy and Tuberculosis. By T. SUGAI, M.D.	30
Status Lymphaticus. By DOUGLAS SYMMERS, M.D.	40
A Study of Ochronosis. By N. W. JANNEY, M.D., PH.D., CAPT., M.R.C.	59
Relation of the Physical Signs to the Roentgen Plate in Pulmonary Tuberculosis. By J. J. SINGER, M.D.	68
A Case of Congenital Absence of the Uterus with Anomalous Vulvovaginal Anus. By E. J. STRICK, M.D.	75
Clinical Experience with Koga's Cyanocuprol. By T. I. MASUDA, M.D., and T. K. MATSUDA, M.D.	78
Vaginal Metastoses of Hypernephroma. By GEORGE GELLHORN, M.D., F.A.C.S.	94
Recent Developments in Intestinal Bacteriology. By ARTHUR ISAAC KENDALL, S.B., PH.D., DR.P.H.	157
Frequency of Protozoic Enterocolitis in the Middle West: Clinical Manifestations, Diagnosis and Treatment. By FRANK SMITHIES, M.D., F.A.C.P.	173
Effect of Stimuli from the Lower Bowel on the Rate of Emptying the Stomach. By FRANKLIN W. WHITE, M.D.	184
Primary Carcinoma of the Vermiform Appendix. A Report of 12 New Cases Occurring in 10,651 Specimens, with a Summary Including 5 Previously Reported Cases Among 2500 Specimens. By STANLEY P. REIMANN, M.D.	190

Two Cases of Suprarenal Disease. By OLIVER T. OSBORNE, M.D.	202
Magnesium Sulphate Solutions in the Treatment of Spastic Contractures of the Rectum and Sigmoid Colon. By HORACE W. SOPER, M.D.	205
Sarcoma of the Heart. By I. PERLSTEIN, M.D.	214
Studies in Cholelithiasis. I. The Disturbances of the Cholesterin Metabolism as a Factor in Gall-stone Formation. By MARCUS A. ROTHSCHILD, M.D., and ABRAHAM O. WILENSKY, M.D.	239
Some Clinical Observations on the Lingual Tonsil, Concerning Goitre, Glossodynia and Focal Infection. By GREENFIELD SLUDER, M.D.	248
Focal Necrosis of the Adrenal Gland: with Remarks upon Acute Adrenal Insufficiency. By ELI MOSCHCOWITZ, M.D.	313
Side-lights on Multiple Myeloma. By ARTHUR WILLIAM MEYER, M.D., and ROBERT E. SWAIN, PH.D.	329
Meningitis in the Newborn and in Early Infancy. By MOSES BARRON, M.D.	358
The Prognosis of Exophthalmic Goitre. By E. MACD. STANTON, M.D., F.A.C.S.	369
The Clinical Display of Syphilis of the Nervous System. By JOSEPH COLLINS, M.D.	375
"Pudendal Hernia." By ALEXIS V. MOSCHCOWITZ, M.D.	394
Studies in Cholelithiasis. II. The Clinical Relationships of the Cholesterinemia to the Pathological Process. By ABRAHAM O. WILENSKY, M.D., and MARCUS A. ROTHSCHILD, M.D.	404
A Huge Hemangioma of the Liver Associated with Hemangiomata of the Skull and Bilateral Cystic Adrenals. By RALPH H. MAJOR, M.D., and DONALD R. BLACK, M.D.	469
An Operable Tumor Involving the Gasserian Ganglion. By CHARLES H. FRAZIER, M.D., Sc.D.	483
Sahli's Volume Sphygmobolometer: an Improvement Over the Older Pressure Sphygmobolometer. By NATHANIEL BOWDITCH POTTER, M.D.	490
The Diagnosis of Chronic Appendicitis. By WILLIAM FITCH CHENEY, M.D.	494
Multiple Neurofibromatosis (von Recklinghausen's Disease) and its Inheritance. By SAMUEL A. PREISER, M.D., and CHARLES B. DAVENPORT	507
The Teeth and Tonsils as Causative Factors in Arthritis. By ROLAND HAMMOND, M.D.	541

Experimental Lesions in the Cervical Sympathetic Ganglia in Relation to Exophthalmic Goiter. By LOUIS B. WILSON, M.D.	553
A Statistical Study of the Relationship of the Origin of Ectopic Contractions to Ventricular Preponderance as Shown by the Electrocardiograph. By ARTHUR E. STRAUSS, S.B., M.D.	557
Studies in Cholelithiasis. III. The Immediate Effect of the Various Types of Operations upon the Cholesterinemia. By ABRAHAM O. WILENSKY, M.D., and MARCUS A. ROTHSCHILD, M.D.	564
New Diagnostic Sign of Foreign Body in the Trachea or Bronchi, the "Asthmatoid Wheeze." By CHEVALIER JACKSON, M.D.	625
Consideration of the Methods for Demonstrating Tubercle Bacilli in the Urine. By ERNEST M. WATSON, M.D.	636
Blood-pressure and Kidney Function Findings in Orthostatic Albuminuria. By E. H. MASON, M.D., and R. J. ERICKSON, M.D.	643
Studies in Fractional Estimation of Stomach Contents. By BURRILL B. CROHN, M.D.	656
Autoserotherapy in Tuberculous Pleurisy. By J. CURTIS LYTER, M.D.	665
Relation of Housing to Pulmonary Tuberculosis. By FRANK F. D. RECKORD, M.D.	670
Focal Infections in Childhood. By SANFORD BLUM, M.D.	681
Comparative Value of Radium and Roentgen Radiation. By RUSSELL H. BOGGS, M.D.	690
Influence of Radium Water Therapy on Creatinin and Uric Acid Metabolism in Chronic Arthritis. By F. H. McCRUDDEN, M.D., and C. S. SARGENT, S.B.	702
Concerning the Anatomy of the Coronary Arteries. By FRED M. SMITH, M.D.	706
Fat Redistribution in the Hypophyseal Type of Dystrophy Adiposogenitalis. By HARVEY G. BECK, M.D.	711
Complement-fixation in Hodgkin's Disease and Allied Affections. By H. T. KRISTJANSON, M.D.	720
The Early Diagnosis of Lead Poisoning, with Special Reference to Abdominal Pain. By GEORGE L. APFELBACH, A.B., M.D.	781
The Opaque Meal Versus the Stomach Tube in the Diagnosis of Gastric Hypomotility. By I. H. LEVY, M.D.	795

Aplastic Anemia. By J. P. SCHNEIDER, M.D.	799
The Diagnosis and Treatment of Diaphragmatic Pleurisy: with Report of Cases. By T. H. KELLY, B.S., M.D., and H. B. WEISS, A.B., M.D.	808
The Fractional Examination of the Duodenal Contents. By MAX EINHORN, M.D.	817
Certain Aspects of the Clinical Value of the Estimation of Kidney Function. By EDWARD H. MASON, M.D.	830

WAR MEDICINE

A Report of Thirty Cases of Meningococcic Cerebrospinal Meningitis. By GUTHRIE McCONNELL, MAJOR, M. R. C., MYRON L. MORRIS, MAJOR, M. R. C., and NEWTON A. SEEHORN, CAPTAIN, M. R. C.	105
Surgical Treatment of War Wounds. By C. L. GIBSON, M.D.	253
Cerebrospinal Fever. By FRANK MARINO, M.D., M. R. C.	270
The Work of the Bureau of Tuberculosis in France—American Red Cross. By WILLIAM CHARLES WHITE, Chief of Bureau	415
Reinfection with Streptococcus Hemolyticus in Lobar Pneumonia, Measles and Scarlet Fever. By LOGAN CLENDENING, M.D.	575
A Memorandum on Milk. By DOROTHY REED MENDENHALL, M.D.	586
Hyperthyroidism in the Recruit. By MAJOR HARLOW BROOKS, M.C.	726
Effects of "Mustard Gas" on the Eyes. By GEORGE S. DERBY, M.D.	733
Influenza Epidemic in Soldiers. By SAMUEL BRADBURY, M.D.	737
Open Pneumothorax: its Relation to the Treatment of Empyema. By MAJOR EVARTS A. GRAHAM, M. C., and CAPTAIN RICHARD D. BELL, M. C.	839
Irritable Heart or Effort Syndrome. By CAPTAIN THAYER A. SMITH, M. C., and MAJOR DAVID BOVAIRD, M. C.	872
Clinical Report upon Cases of Lobar Pneumonia Treated with Antipneumococcus Serum as Observed at General Hospital No. 6, Fort McPherson, Georgia, October, 1917, to May, 1918. By LIEUT.-COLONEL C. N. B. CAMAC, M. C., U. S. A.	887

REVIEWS

Reviews of Books	121, 276, 434, 593, 741
----------------------------	-------------------------

PROGRESS OF MEDICAL SCIENCE

Medicine	745, 894
Surgery	127, 285, 439, 603, 748, 895
Therapeutics	131, 288, 442, 754, 900
Obstetrics	135, 291, 445, 607, 759, 902
Gynecology	296, 449
Ophthalmology	141, 299, 452
Otology	144, 302, 455, 611
Dermatology	458
Pathology and Bacteriology	147, 305, 460, 614, 769
Hygiene and Public Health	151, 308, 464, 620, 774, 908

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

JULY, 1918

ORIGINAL ARTICLES

**THE ANCIENT FACTORS IN THE RELATIONS BETWEEN THE
BLOOD PLASMA AND THE KIDNEYS.¹**

BY A. B. MACALLUM, M.D., F.R.S.,

PROFESSOR OF BIOCHEMISTRY IN THE UNIVERSITY OF TORONTO.

THE animal organism, except that of the unicellular type, is a congerie of organs whose history, individually considered, as it is thus far revealed, constitutes the sciences we call comparative embryology and comparative physiology and which we must know, not only to comprehend the full significance of the work they now perform, but also to recognize and interpret the possible variants from the normal in function and structure which they may manifest. This history, in invertebrates as in vertebrates, is one of change either in structure or in function, or, often, in both structure and function, and, accordingly, frequently confusing and difficult to follow in any attempt to gain a full comprehension of the conditions and forces that determined the character of each organ.

One needs but to scan the list of the organs of the vertebrate body to illustrate how true this is. The nervous system with its protean manifestations in the line of evolution, the thyroid, the thymus, the suprarenals, the pituitary body, the pineal gland, the gills, the lungs, the alimentary canal with its accessory structures and even the liver, all have a past in which the dominant feature has been changed in structure and function with the result that the final stage in each transcends the earlier ones and so obscures their

¹ The Hatfield Lecture delivered before the College of Physicians, Philadelphia, April 10, 1917.

characters that it is now difficult to determine the earlier history except in some cases from the structural side.

One thing is indeed certain. The change has never been of the *per saltum* type. But it has been unceasing, without pause, and it is progressing today, as it has been in the long past. The Heraclitan flux therefore plays its part in organogenic evolution as distinctly as it does in the physical world.

Among all the organs with their varied history as to structure and their variations in function, there is, however, one whose function in one particular respect has not changed from the time when it first began to evolve in the very far past. This organ is the kidney and the function which it performs, as it has performed it far back in the very beginning of the history of vertebrate life, is the regulation of the inorganic composition of the internal medium of the body, which we know as the blood plasma.

This organ was among the very first to appear in the protovertebrate, or in the first invertebrate type which began to differentiate along the line of development which resulted in the appearance of the protovertebrate in the Cambrian, or it may be pre-Cambrian times. If we may rely on the order in which the organs appear in the embryological history of the vertebrate, the renal organ is as ancient as the neural canal, and its origin would appear to antedate by a long period the closure of this canal and the disappearance of the coelomic cavity into which the primitive nephric tubules opened. If the latter are, as has been claimed, derived by differentiation from the coxal glands of a crustacean-like form, they are of more ancient origin than the neural canal itself.

What the kidney of the protovertebrate was we may gather from the earliest form of the vertebrate kidney, which consisted of three divisions, arranged in order from before backward: the pronephros, the mesonephros and the metanephros. One of these, the mesonephros, becomes the adult kidney in fishes and amphibia; another, the metanephros, becomes the functional kidney in other vertebrate classes, reptiles, birds and mammals. This is of significance, as I shall show later, in indicating that the regulation of the inorganic composition of the blood plasma exercised by the adult kidney must have been exercised also by the kidney of the protovertebrate.

In order to understand what this regulation involves we must for a moment consider what the inorganic composition of the blood plasma is. The salts of the blood plasma in amount range between 0.78 and 0.88 per cent. of the weight of the plasma, and they consist of the chlorides, phosphates, carbonates and sulphates of sodium, potassium, calcium and magnesium. The salts of sodium are by far the most abundant, after which come those of potassium, calcium and magnesium in the order mentioned. The salts of sodium, chiefly the chloride, amount to more than 90 per cent. of the total inorganic solids of the plasma.

The composition in detail has been determined by Bunge for the horse, ox and pig, and by Abderhalden for the ox, horse, pig, sheep, dog, cat.

The composition of human plasma has not been redetermined since 1850 when Carl Schmidt published the results of a number of analyses which are quoted now in all the text-books. They were obtained by the methods in use seventy to eighty years ago, which gave less exact determinations than those now followed in making such analyses, and, consequently, the percentages, notably those of potassium, calcium, magnesium and chlorine, which Schmidt's determinations yield, are open to question.

The inorganic composition of the plasma in birds, reptiles and amphibia has not been ascertained, but the total percentage of the ash has been ascertained to range between 0.8 and 0.9 in birds and reptiles, while in the frog it has been estimated to be as low as 0.46, but this may possibly be due to the difficulty of getting enough of the plasma of the frog free from admixture with water or lymph. The fact that in birds and reptiles the percentage of the salts is as high as in mammals is an indication that the details of the composition are not widely different from those of the plasma of the mammals above mentioned.

The analyses of the blood plasma in fishes which we have today are only those of the cod, pollock and dogfish, which I made eight years ago, and they are of special interest in connection with the analyses of the blood plasma of mammals.

If one examines Bunge's and Abderhalden's tables, giving the results of their analyses, one is impressed only with the fact that the details obtrude themselves to the exclusion of all else, that in fact one does not see the woods for the trees, and, in consequence, the significance of the results are obscured.

If, however, one selects the cationic elements and arranges them in values proportional to the most abundant one, sodium, which may be made equal to 100, order is obtained from the maze of details in these analyses, and one finds surprising resemblances in the values obtained from plasmas of all the mammals. Further, the proportions obtained from the analyses of the plasma of the fishes referred to fall into line with those from mammals in such a way as to suggest that we have thus revealed a cardinal feature in the inorganic composition of the blood plasma of vertebrates.

This feature is indicated in the following table of ratios in which Na = 100.

	Na.	K.	Ca.	Mg.
Dogfish (<i>Acanthias vulgaris</i>)	100	4.61	2.71	2.46
Cod (<i>Gadus callarias</i>)	100	9.506	3.93	1.41
Pollock (<i>Pollachius virens</i>)	100	4.33	3.10	1.46
Dog	100	6.86	2.52	0.81
Mammal (average)	100	6.69	2.58	0.80
Man (C. Schmidt)	100	9.22	3.37	1.76
Man (A. B. M.)	100	6.11	2.71	0.85

The ratios for man are derived from Schmidt's analyses carried out, as already stated, with methods which were less exact than those which are employed today, and, in consequence, they are accepted with reserve, more especially as in my own determinations on the blood plasma of man the values for potassium, calcium and magnesium are much lower than those given by Schmidt and in general accord with those of Abderhalden and Bunge for mammals.

The ratio of potassium in the blood plasma of the cod, as determined in my own analyses, is high, but this may possibly be due to hemolysis, the preparation of serum which I used having a reddish tinge and therefore probably contained the potassium of the hemolyzed corpuscles, which thus would give a higher ratio for this element than would be given by pure plasma or serum. The fact that so near a relative of the cod, as is the pollock, gives less than half the ratio of the cod and approaches very closely that of the dogfish supports the view that the ratio in the cod is less than that given above.

Apart from these exceptions, if they are to be ranked as such and not due to errors in analysis or to abnormal composition, the striking feature is the very extraordinary parallelism between the ratios in mammals and those in fishes. This parallelism appears enhanced when one considers that the concentrations of inorganic salts in both classes of vertebrates differ. The concentration in the serum of the mammal, as already stated, ranges from 0.78 to 0.88 per cent. in the sera of the cod and pollock, from 1.282 to 1.293, respectively, while in the dogfish it is 1.774, or practically, double what it is in the serum of a mammal.

The parallelism in the ratios of the individual elements in the highest as well as in the lowest vertebrates is a cardinal fact, something more fundamental than the total concentration of the salts in the plasma. Its occurrence in two such widely separated classes of vertebrates suggests that it is an endowment received from the common ancestor of both, the protovertebrate, which must have existed in the early Cambrian or pre-Cambrian times.

What is the explanation of these ratios between the sodium, potassium, calcium, and magnesium?

The answer to this question I obtained some fourteen years ago when determining the inorganic composition of certain medusæ and comparing it with the composition of the ocean water of their habitat. *Aurelia flavidula*, the common jelly fish of our coasts in July and August, when it is liquefied, which happens when it is allowed to stand in a dry dish, furnishes a liquid in which, besides organic constituents, is contained a concentration of inorganic salts like that of the ocean water from which the animal was taken. From the analyses of its salts, compared with those of ocean water, ratios between the sodium, potassium, calcium and magnesium (with Na = 100) were obtained which revealed a very striking parallel.

	Na.	K.	Ca.	Mg.
Ocean water (Dittmar) . . .	100	3.63	3.91	12.10
<i>Aurelia flavidula</i> (Macallum)	100	5.18	4.13	11.43

The parallelism between the two series of ratios is very close and the conclusion follows that the fluid in the tissues of *Aurelia* is but very slightly modified ocean water and of the same concentration as the latter.

It was, however, when the ratios for sea water were compared with the ratios of the blood plasma of a mammal, for example, the dog, that one obtained a clue to the origin of the ratios in the blood plasma of vertebrates. We see in the latter:

	Na.	K.	Ca.	Mg.
Ocean water (Dittmar) . . .	100	3.61	3.91	12.10
Dog (Abderhalden)	100	6.86	2.52	0.81
<i>Limulus polyphemus</i> (Macallum) .	100	5.62	4.06	11.20
<i>Homarus americanus</i> (Macallum)	100	3.73	4.85	1.72

that the ratios are parallel to those of ocean water, except in regard to magnesium. Were the ratio of the latter reduced to 1, or thereabouts, the parallelism between the two series would be so striking as to render unnecessary further discussion of the question of the origin of the ratios in the blood plasma.

That these ratios are of oceanic origin can admit of no doubt when we compare them with those of the horseshoe crab and lobster.

The horseshoe crab, *Limulus polyphemus*, which has had its habitat in the ocean since its origin in the early portion of the Palæozoic age, has a plasma in which the parallelism between it and ocean water is uncontroversible. This is no doubt due to the fact that the osmotic pressure of the ocean has been acting on its plasma through the many millions of years which have elapsed since the Cambrian age, and, though unquestionably the ocean has been undergoing, in all that time, changes, not only in concentration but also in the ratios of its salts, the blood plasma of the horseshoe crab has kept pace with it and today the concentration of its salts equals that of the ocean water in which it lives, and the ratios in its plasma are practically those of ocean water. We thus see that ocean water does in this one case determine the inorganic composition of the blood plasma.

In the plasma of the lobster, *Homarus americanus*, which has been associated with the ocean only since the Cretaceous period, though the concentration of the inorganic salts is as high as the ocean water of its habitat, the ratio of the magnesium only is different from that of the ocean.

In both the lobster and the horseshoe crab the concentration of the inorganic salts of the plasma appears to vary with the concentration of the ocean water of their habitat, and in brackish water it falls to that of the latter. The concentration of the salts of the

plasma in these forms follows the concentration of the medium, whereas in the Selachians, which include the sharks and the dogfish and which have had their habitat in the ocean ever since the early part of the Palæozoic age, the concentration of the plasma salts exceeds half that of ocean water to a slight extent, although the osmotic pressure of the ocean has been exerting its effect on the Selachian plasma for at least several scores of millions of years. In the marine Teleostean fishes, which, like the cod, have been denizens of the ocean for a time, perhaps, not half as long, the concentration in the plasma is but little more than a third of the concentration of the salts in the ocean.

In the marine invertebrates of today the circulatory fluid is but a more or less modified form of sea water. In some the circulatory channels freely communicate with the exterior with the result that the circulatory fluid is pure sea water, but, even when the circulation is closed as it is in the horseshoe crab, the blood plasma is sea water with proteins and other organic constituents.

There is then a profound difference between the blood plasma of vertebrates and that of invertebrates. That of the latter varies more or less readily with an immediate change in the medium of the habitat, while that of the former is affected, and then but appreciably, only after millions of years.

Are we then to conclude that the plasma of vertebrates was primarily of origin different from that of the plasma of invertebrates?

If we scan the tables of ratios for the sodium, potassium, calcium and magnesium in the plasmas of the different forms of vertebrates and invertebrates, we see in the parallelism already referred to an unmistakable indication that the blood plasma of vertebrates was also originally sea water, not indeed the sea water of the present age, but of a far past when the concentration of its salts was less than one-third of what it is now and when also the potassium was relatively more and the magnesium relatively less abundant than in the ocean of today.

The sea is the original home of all life on our globe, and it was in the sea that the differentiation between animal and vegetable life as well as the evolution of the great divisions of the animal kingdom were effected. Indeed, the great events in the evolution of animal forms have been rendered possible by changes which have taken place in the composition of the ocean. Among the fundamental results of these changes was the development of a closed circulatory system of vertebrates, the fluid contained in which became henceforth independent of the composition of the contemporary ocean, and, as we have seen, of the ocean of subsequent periods even after many millions of years, as in the case of the Selachians (sharks), marine Teleosts (cod, herring) and the Cetacea (whales).

The sea ever since the first condensation of water on the original

cooled rock crust of our globe has been changing in composition by the leaching out of its bed the salts it contained and by receiving salts in the river discharge, also leached from the land areas of the globe. The quantity of salts annually discharged from the land areas is enormous and it is estimated by Joly at about one hundred and fifty-seven millions of tons (157,270,000), which, if divided into the amount of salts which he calculates as contained in the ocean today, namely, 14,151,000,000,000,000 tons, would give the age of the ocean as approximately ninety million years. The concentration has therefore been slowly changing and it must have been in the far past much less than it is now.

The relative proportions of the various salts must have changed also. All the salts discharged in the ocean by the rivers have not been retained, for, were they retained, the potassium and the calcium salts would be very greatly more abundant than they are now. Indeed the calcium salts in the ocean would have long ago reached a degree of high supersaturation quite impossible to conceive of, since the lime salts in the calcareous rocks of the earth's crust, deposited from sea water in the past ages, would thus be in solution in the sea. The potassium was, once, relatively to the sodium, more abundant than the present ratio indicates, and it has been and is being constantly extracted from the ocean in the formation of such minerals as *glauconite* apparently at a rate which keeps its concentration over long ages fairly constant. The magnesium salts also have been concentrating slowly, for the elimination of magnesium as carbonate in the formation of dolomitic limestone has been proceeding at a rate less than that of the constant addition through the river water. This would postulate that magnesium is not only absolutely but also relatively more abundant in the ocean of today than it was in that of the far past.

The only constituents that are not extracted from the ocean are the sodium salts. These have always therefore been on the increase from a time in the early pre-Cambrian when they were perhaps but slightly in excess of those of potassium. Their increase will proceed in the ages to come and finally produce such a degree of concentration and, consequently such a specific density that will, as in the water of the Dead Sea, permit the human body to float because of its lower specific gravity.

The differences in the series of ratios exhibited by the sodium, potassium, calcium and magnesium in the blood plasma of vertebrates on the one hand and in the sea water of today, on the other, parallel as these two series so strikingly are, can be explained as due to the blood plasma reproducing, approximately, the ratios obtaining in the ocean of the time when the original ancestral form of vertebrates, the protovertebrates, or eovertebrates, arose. The total concentration of the salts in the blood plasma can also be explained as due to a reproduction of the concentration of the sea

water of the same age, that is, when it had less than 1 per cent. of salts.

How far back in geological time this period was it is difficult to determine exactly. It must have been earlier than the earliest or most ancient fossil remains of vertebrates indicate, that is, in the earlier Cambrian or even pre-Cambrian, for the protovertebrate must have long preceded the vertebrates to which, through evolution, it gave origin. How long the intervening period has been is also difficult of determination. Estimates made on various bases give different results and the only satisfaction that one obtains from them is the recognition of their extreme limits, the maximal and minimal. Prof. Strutt in determining the content in helium of a mineral derived from Cambrian rocks of Renfrew County, Ontario, Canada, calculates that it was over seven hundred million years old. If, on the other hand, one follows Joly's method, based on the amount of salts in annual river discharge into the ocean, and the amount now in the ocean, and also accepting as approximately correct the percentage of salts in the ocean when the protovertebrate arose as less than 1 per cent., and therefore less than one-third of the concentration in the ocean of today, it follows that more than sixty millions of years must have elapsed since the protovertebrate appeared and disappeared on the geological horizon.

Whether we accept the higher or the lower estimate, or even a lower one still, the enormously long period during which the blood plasma has been simulating Palæo-oceanic conditions in the concentration of its salts and in the ratios of the sodium, potassium, calcium and magnesium it contains, emphasizes the importance in one respect of the organ which has maintained through the long ages of vertebrate history this concentration and these ratios, practically unchanged.

This organ is the kidney. There is in invertebrates no structure with a similar function or with a function even distinctly approaching that of the vertebrate kidney. It is this organ that has made a fundamental difference between the vertebrate and the invertebrate, not only in the struggle for existence but also in the capacity to evolve higher forms of animal life. The animal form that must accommodate its internal medium to that of its habitat has an enormous handicap when it changes its environment, from ocean to fresh water or to land, as compared with one whose internal medium, under all circumstances, is constant in composition. With such a handicap vertebrate life and all that it involves would have been impossible.

This function of the kidney is fundamental and is more ancient than that of excreting the waste products of the tissues of the body. In the dogfish, as in Salachians generally, whose history has been associated with the ocean since their origin in the Silurian period and in whose blood plasma the concentration of salts has in

consequence been increased to only about half that of the sea, the difference between the osmotic pressure of the ocean water and that given by the salts of the blood plasma is equalized by urea which amounts to more than 2 per cent., and by ammonium salts, which amounts to more than $\frac{N}{10}$ reckoned as NH_3 . This retention of urea and ammonium salts undoubtedly developed as a result of the tendency of the blood to balance the slowly increasing osmotic pressure of the sea water. The very fact that the kidneys in these forms exhibit inertness in the elimination of urea while they are extremely active in the elimination of salts is extremely significant. What they do most rigorously is the regulation of the inorganic composition of the blood, therefore the more firmly fixed physiological habit must be the more ancient one and, consequently, their earliest function was not the elimination of waste metabolic products but the regulation of the inorganic composition of the blood plasma. The function of excreting waste products developed later and in Selachians never acquired the fixity that characterizes the other function.

In the long ages the kidney has thus performed a function which for constancy and unvarying regularity is unrivalled in the world of life. This constancy, this unvarying regularity contrasts strikingly with the variation in function which the other organs have undergone and indicates how basic the kidney is in the vertebrate system and why it takes precedence in the body as a vertebrate organ *par excellence*.

How it happened that the kidney in the protovertebrate acquired this fixity of function we do not know. Geologists concede a very long time to the pre-Cambrian, a duration which, according to different estimates, ranged from one-third to nine-tenths of the whole geological period. In this long cycle of time many things could have happened and conditions must have obtained which impressed on the primitive kidney of the protovertebrate an abiding character, not to disappear even though the original organ underwent a marked transformation in structure before it developed into the renal organ of the vertebrate of today.

The question now arises, whether this Palæo-oceanic character is ever disturbed in disease of the kidney and, if it is, what are the results.

To this question there is not much to offer in the form of an answer. There have been very few investigations of the inorganic composition of the blood plasma in disease, and these only of a very limited scope, bearing almost wholly on the chlorine content, the amount of which was supposed to give an indication of the total concentration and of the sodium present. The conclusions based on such analyses are, of course, accepted only with reserve simply because of the tenuity of the data on which they are based. Plasma that are accessible are those of Schmidt.

Believing that the subject had possibilities in a clinical line, I undertook during the last five years investigations on the inorganic composition of normal human plasma, with a view to comparison of the same with the blood plasma in cases of Bright's disease, and, more especially, in cases of puerperal eclampsia. These investigations are not yet completed, owing to the time-devouring character of the work involved, but some of the results so far obtained are definite and interesting and they may be mentioned here.

It is to be premised, first of all, that the determinations in Schmidt's analyses, so far as sodium, potassium, calcium and magnesium are concerned, give too high values. Those for sodium range from 0.3173 to 0.3438 per cent. and for potassium from 0.0314 to 0.0332, while in my analyses the range of sodium is from 0.29 to 0.316 and of potassium from 0.019 to 0.0212. It may thus be seen that Schmidt's values are quite too high, and especially in the case of potassium, his average for the latter being 60 per cent. in excess of mine. The results obtained for the plasma in Bright's disease are quite incomplete, but those for puerperal eclampsia are far enough advanced to enable me to give some points of interest.

In 4 cases the ratios on the bases of Na = 100 were:

Cases.	Na.	K.	Ca.	Mg.
1	100	17.66	4.02	3.42
2	100	26.70	3.27	2.37
3	100	10.60		
4	100	10.10	2.59	0.68
15 (normal)	100	6.11	2.71	0.85

The magnesium and calcium content is high in Cases 1 and 2 and normal in No. 4, but in all the potassium is in excess and in No. 2 extraordinarily so, as much as four times the normal, while in No. 1 it is nearly three times the normal.

There was a minute quantity of hemoglobin in the serum of all the four cases, as revealed by the spectroscope, and some of the potassium found in excess of the normal may have been derived from hemolyzed red corpuscles which are rich in potassium salts, but this would not explain the excess in No. 2, in which the amount of hemoglobin in the serum did not exceed that in Nos. 3 and 4. It is possible that hemolysis in the circulating blood may be responsible ultimately for this excess, but this does not explain the non-elimination of the potassium in excess above normal by the kidneys. Temporarily, at least, in eclampsia the cellular elements of the kidney concerned in maintaining the normal ratio of potassium in the blood plasma must suffer a partial or total eclipse of function.

I am inclined to infer from the results of my observations that the very first change from the normal to the definitely established primary condition in some of the forms of Bright's disease is a loss of the power to maintain the Palæo-oceanic ratios.

The structures in the kidney involved in maintaining these ratios

are the proximal convoluted tubules, which, with the glomeruli, are derived from and therefore represent the original parts of the kidney of the earliest vertebrates and of the protovertebrates. The proximal convoluted tubules are also concerned in reducing the H-ion concentration of the blood, for they secrete acid, not acid salts, into the urine, a function which is also very ancient, a function performed in invertebrates by all the cells of the body situated near the body surface, and still performed intermittently and with a high degree of specialization by the gastric glands of vertebrates. In some invertebrates other tissues have specialized in this matter also, as for example, in the salivary glands of the carnivorous mollusc *Dolium galea*, the concentration of the sulphuric acid of the "saliva" of which exceeds 4 per cent.

It may be that the function of preventing the ever-tending-to-increase of the H-ion concentration of the blood plasma is as ancient as the Palæo-oceanic function, a view which their common localization in the proximal tubules supports.

Enough has been said here to emphasize the view that behind the functions of the renal organ is a history which links up the human body with the far past with an age of the earth when its oceans contained only what would now be regarded as brackish water and the earliest type of vertebrate life was just beginning to appear as a marine form. From the facts advanced it will be gathered also that the blood plasma, so far as its inorganic salts are concerned, is but a reproduction of the remotely ancient ocean, and that it is an heirloom from the life in

"that immortal sea
Which brought us thither,"

not indeed in the Wordsworthian sense, but in the literal one, for the sea is the original home of all life on the globe and gave our blood, and, accordingly, the tissues of our bodies, a character that long ages have not effaced and will not efface.

TYPHOID VACCINE IN A CASE OF TYPHOID SPINE.

By W. ALLAN, M.D.,

VISITING PHYSICIAN TO PRESBYTERIAN HOSPITAL,

AND

J. W. SQUIRES, M.D.,

ROENTGENOLOGIST, PRESBYTERIAN HOSPITAL, CHARLOTTE, N. C.

As only 30 out of the 104 cases of typhoid spine reported up to this time have been accompanied by roentgenograms, we feel justified in reporting a case with positive roentgen findings, and so

far as we have been able to discover, typhoid vaccine has not been used before in the treatment of this condition.

Few medical subjects have been so constantly and so thoroughly reviewed as typhoid spine, so that in reporting this case only a very brief summary of the development of our present knowledge on this subject will be given. Gibney,¹ in 1889, first called attention to the stiff and painful back which occasionally follows typhoid fever. However, his "Austrian Tyrol" case, with symptoms lasting two years, followed by permanent wry-neck, rather confused typhoid spine, with other types of spondylitis. Gibney reported this case to support his view that typhoid spine is a definite, infectious (inflammatory) process; this case is condemned by Lord² but approved by Halpenny.³

A few years later the waters were muddied when Osler⁴ reported 4 cases of typhoid spine as simple neuroses. Inasmuch as post-mortem pathology was not available in this condition, this conclusion could not be eliminated until some years later, when the roentgen rays began to demonstrate bony changes that are apparently responsible for the pain and the nervous symptoms. Lord, in 1902, reviewed the 26 cases reported up to that time, and concluded that the "pathology seems to be a perispondylitis or spondylitis, or both," and that although a few cases might be simple neuroses, "the coexistence of a deformity and nervous symptoms in one-half of the neurotic cases suggests that all the neurotic cases may be organic as well." At that time only Cutler's⁵ case had been radiographed and no bony changes were found.

In 1905 Fluss⁶ reviewed the subject, finding 46 cases. The next year T. McCrae⁷ reported 2 cases with roentgenograms and was the first to give roentgenographic proof of the new-bone formation which usually occurs. Halpenny reviewed the subject very thoroughly down to December, 1908, summarizing 73 cases, and Elkin and Halpenny⁸ have reviewed an additional 22 cases occurring up to the end of 1913, making a total of 95 cases.

In 1914 Conklin⁹ and Job¹⁰ each reported 1 case; in 1915 Galli,¹¹ Wilcox,¹² and Rugh¹³ reported single cases and Carnett¹⁴ reported 4 cases; we have found no cases reported during 1916.

Typhoid spine comes on within three months after typhoid fever

¹ New York Med. Jour., 1889, i, 596-598; Tr. Am. Orthop. Surg., 1889, ii, 19.

² Boston Med. and Surg. Jour., 1902, cxlvi, 26, 689-691.

³ Surg., Gynec. and Obst., 1909, viii, 649.

⁴ John Hopkins Hospital Bull., xxv, 265; *ibid.*, iv, 73 and v, 315.

⁵ Boston Med. and Surg. Jour., 1902, cxlvi, 26, 687-689.

⁶ Centralbl. f. Grenzgeb. der Med. u. Chir., 1905, viii, 645.

⁷ AM. JOUR. MED. SC., 1906, cxxxii, 878-889.

⁸ British Jour. Surg., 1914, i, 4, 602-609.

⁹ Med. Record, 1914, lxxxv, 4.

¹⁰ Bull. et mém. Soc. méd. de hôp. de Paris, 1914, xxx, 990.

¹¹ Münch. med. Wehnschr., April 13, 1915.

¹² Colorado Med., 1915, xii, 7.

¹³ Am. Jour. Orthop. Surg., 1915, xii, 2.

¹⁴ Ann. Surg., April, 1915.

either suddenly or gradually, with pain in the back, which is apt to be severe. The character of the preceding fever is without significance. Three-fourths of the sufferers are males, and a history of more or less trauma is usually to be obtained. The lumbar spine is the site of election and the pain may radiate to the front of the body and down the legs. Movement of the spine is exquisitely painful, so that the back is held rigid, and sleep is very much broken by relaxation at night. Spasm of the muscles is frequent and abdominal rigidity has been observed. Carnett reports rhythmic contraction of the abdominal muscles. Tenderness over the spine is common, with occasional hyperesthesia, ankle-clonus, increased knee-jerks and muscular atrophy. After much suffering the victims become very neurotic. Half the cases have fever of an irregular type and the leukocyte counts reported have varied from 6000 to 17,600. About half the cases develop deformity, varying from slight prominence of one or several vertebral spines to marked kyphosis or scoliosis, a small number of these deformities being permanent. The duration of symptoms ordinarily is from three to five months, and no recurrences have been reported. Under rest, either postural or mechanical, tonics and the cautery all patients have completely recovered, except that in a small number permanent deformity with some limitation of motion has persisted.

In 11 cases of typhoid spine examined roentgenographically, reviewed by Halpenny,¹⁵ the findings have varied from gross bony changes to none at all. Connor, Lovett, McCrae, Silver and Weigel report a total of 8 cases, with distinct changes of either the vertebræ, intervertebral disks or vertebral ligaments. Cutler and Petteshon in their cases found nothing abnormal. In 2 cases McCrae found deposits of new bone. In the first it filled the intervertebral space between the second and third lumbar vertebræ, apparently being deposited in the lateral ligaments and forming bony union; in the second the process extended from the second to the fifth lumbar vertebræ and appeared to involve both the lateral ligaments and part of the intervertebral disks. In the first of Myer's cases a synostosis between the second and third lumbar vertebræ, with loss of height from disappearance of the intervertebral space, was observed. In his second case there was clearly a synostosis of the eleventh and twelfth dorsal vertebræ, with diminution of height, owing to disappearance of this intervertebral space. In Silver's case the vertebral bodies seemed to be of normal thickness, but the space between them, corresponding to the disks, was absent, and the shadow of the first lumbar vertebra passed directly into that of the second; over this area there was increased density. On the right the lateral borders of the vertebral bodies formed an unbroken curved line; on the left there

¹⁵ Loc. cit.

was an irregular shadow projecting outward between the transverse processes.

Elkin and Halpenny¹⁶ review an additional 14 cases examined roentgenographically by various investigators, in 2 of which nothing was found. Of this series they cite Sireday's case, in which there was found thickening of the left side of the vertebral column of the second, third, and fourth lumbar vertebræ. In the other cases there were changes in the disks. Goddu found changes in the last dorsal and first lumbar vertebræ. Sweet found the disks gone between the fourth and fifth lumbar vertebræ and new-bone formation. McIntyre found the disk thickened between the fourth and fifth lumbar vertebræ and a deposit of new bone from the spine to the crest of the ilium; in his second case the fourth disk was thickened. Corling and Cain found a dense shadow on the sides of the ninth, tenth and eleventh dorsal vertebræ; a later roentgenogram of this was interpreted as an effusion beneath the periosteum and ligaments.

The cases reported by Wilcox and by Rugh and 3 of Carnett's cases showed the usual bony changes, while one of Carnett's cases showed nothing as late as the eleventh week.

In the case we report the roentgenograms show on the sides of the bodies of the second and third lumbar vertebræ a distinct clasp-like formation of new bone, producing a firm union and also a partial destruction of the disk and slight roughening of the body of the third lumbar vertebræ at the point of origin of the new bone. There is no evidence of involvement of any other vertebræ, though all were taken.

As demonstrated by the roentgen rays the early pathological findings consist in destructive changes in the bodies of the vertebræ, with absorption of the intervertebral disk; later there is proliferation of bone from the periosteum, with bony metamorphosis of the lateral ligaments. As first pointed out by McCrae, some cases may not reach the stage of new-bone formation, and roentgenograms may be negative early in the condition and positive later, as shown by Carnett's third case.

CASE REPORT. MRS. W., white, aged twenty years, married; cotton-mill operative. She was admitted to the Presbyterian Hospital December 5, 1916, complaining of severe pain in the left flank and over the whole region of the left hip. Her family and past history were unimportant, except that she had had an attack of typhoid fever beginning in June, 1916, and lasting for nine weeks. She returned to work in the mill in September. About November 1 her present trouble started as a "catch" in her left hip on walking. This pain became rapidly worse, spreading to her back and hip and thigh, so that she has been confined to bed for the past month. The

¹⁶ Loc. cit.

least movement, as turning in bed, brings on painful spasm of the back muscles. At present the back is better but the pain over the hip and crest of the ilium is worse. From pain and loss of



FIG. 1.—Clasp-like formation of new bone connecting second and third lumbar vertebrae.



FIG. 2.—A, narrowing of vertebral slit from absorption of disk; B, area of erosion on body of third lumbar vertebra.

sleep she has lost appetite and flesh. Temperature from 99° to 100° on admission, with pulse 90 to 110. Her physician says that during the past month she has had high fever, reaching 103°, at times continuous, at other times intermittent.

Examination showed both upper and lower incisor teeth rotted off to the gums, with moderate inflammation of the gum margins. Eyes, throat, glands, heart, lungs, abdomen, skin and reflexes normal. No real or apparent shortening of the left leg. Trochanter below Nélaton's line. Motion of hip-joint normal. The motion of the lower half of the spinal column is very limited indeed. Moderate motion backward and to each side, all causing pain referred to left iliac crest. Cannot bend forward at all. Even when standing quietly the vertebral column is overextended and inclined to the left, with the left lumbar muscles spastic. Gait normal. Palpation over left lumbar back and ilium painful. Sacro-iliac joint not sensitive.

Flexion of extended legs on body equally limited on both sides because of the pain this produced in the back. Jarring the soles of both feet caused pain in the left lumbar region. Roentgenograms of all the teeth and the pelvic bones were normal. The changes in the second and third lumbar vertebræ are shown in the accompanying roentgenograms.

The back was strapped with adhesive and the usual immunizing doses of a commercial mixed typhoid vaccine were given. After the first dose, December 10, the temperature, which had been running from 99° to 100°, remained normal. After the second dose, December 14, she was allowed to return home, and was able to sleep through the night without pain. The third infection was given December 19, at which time the improvement was marked. Reported December 27, showing the back much improved; anxious to go to work.

January 17 the back was no longer painful and motion not much limited. Allowed to return to work. Roentgenograms showed no increase in bone formation.

February 16, she has worked without difficulty, except that her back tires more easily than formerly. No pain and no deformity. Very slight limitation of motion, with about 5 per cent. decrease in efficiency of the back. Roentgenograms showed no further changes.

CONCLUSIONS. It is difficult to estimate the value of the typhoid vaccine in this case, as the process was subsiding spontaneously. However, the temperature remained normal after the first dose, and there was a marked decrease in the pain the day after the second dose. From the clinical history of typhoid spine it seems probable that typhoid vaccine given early, would stop the development of this local infectious spondylitis.

**ELECTROCARDIOGRAPHIC EVIDENCE OF ABNORMAL VEN-
TRICULAR PREPONDERANCE AND OF AURICULAR
HYPERTROPHY.¹**

BY PAUL D. WHITE, M.D.,

AND

ARLIE V. BÖCK, M.D.,

BOSTON, MASSACHUSETTS.

(From the Massachusetts General Hospital, Boston.)

THE present communication summarizes a clinical investigation undertaken to define the electrocardiographic limits beyond which one may conclude the presence of abnormal ventricular preponderance and of auricular hypertrophy.

It has first been necessary to establish an index for the calculations. The following satisfactory formula was finally employed: the measurements are of the amplitudes of the string excursions expressed in tenths of a millivolt (millimeters on the photographic records):

$$(U_1 + D_3) - (D_1 + U_3) = I,$$
²

where *I* signifies *index*, U_1 signifies the amplitude of the chief upward excursion of the QRS group in Lead I_3 , and D_3 signifies the amplitude of the chief downward excursion of the QRS group in Lead III; D_1 and U_3 are interpreted correspondingly.³ For example, if U_1 measures 16 millimeters, D_1 3 mm., U_3 5 mm., and D_3 22 mm., the index = $(16 + 22) - (3 + 5) = +30$; if U_1 equals 4 mm., D_1 18 mm., U_3 19 mm., and D_3 0 mm., the index equals $(4 + 0) - (18 + 19) = -33$.

An increase of the index in the positive direction indicates a swing of the electrical axis to the left either from actual change in cardiac position or from increase of left muscle mass in the heart itself; a change toward the negative values indicates a swing of the electrical axis to the right.

For controls we have examined 100 normal people: 60 young male adults, 20 young female adults, 20 children under nine years of age and 20 old people over sixty-five years of age. Dr. E. B. Krumbhaar has kindly sent us his table of measurements⁴ of 41 children and we have also used the figures of Lewis and Gilder⁵ in

¹ Read in part before the American Society for Clinical Investigation, Atlantic City, N. J., May 1, 1917. The call to active service abroad delays the publication of a detailed report of this investigation with complete tables.

² A similar formula was mentioned by Lewis, Heart, 1914, v, 398.

³ The average of several successive beats should be taken to avoid respiratory variations in amplitude.

⁴ This table has since been published in Heart, 1917, vi, 189.

⁵ Philosophical Transactions of Royal Society, 1912, cccii, B. 351.

their study of 52 normal young male adults. Our high positive and negative indices have been found among 1100 cases electrocardiographed at the Massachusetts General Hospital.

It was of considerable interest to note in the case of the electrocardiogram of old age that not infrequently the index was nearer the average normal value than that of a number of the healthy children with relatively high positive values. When a decidedly high-positive value was found in an old person, marked arteriosclerosis, hypertension or aortic regurgitation was also found. It would seem then that old age *per se* does not give a characteristic electrocardiogram.

The individual electrocardiogram is remarkably constant, as a rule, in the value of the index. In 12 cases the maximum individual variation over periods of three months to two years was found to be +4. In a few cases, more particularly those with aberrant ventricular complexes, as in bundle branch block with progressive heart disease, there may be considerable variation: 3 of our cases—all with aberrant ventricular complexes—showed variations of -25, -17 and -34 in the index over periods of five months to two years. Electrocardiograms of cases such as these cannot be used in the estimation of ventricular preponderance.

In the course of this investigation it was found by comparison of electrocardiograms with fluoroscopic tracings that cardiac position has an important bearing on the index, and a respiratory test has been used. The position of the heart as determined by the type of the individual being studied, for example, squat or lanky, very likely affords the explanation for the occasional discrepancies between ventricular weights and electrocardiograms. Incidentally it may be noted here that the position of the diaphragm has much more influence on the inclination of the actual cardiac axis, and therefore on the electrocardiographic index than have pneumothorax or pleural effusions. These, if large, generally push the heart *in toto* to one side or the other with little or no change in the inclination of the axis; if there is a change in the axis it may actually be due to a greater displacement of the base than of the apex.

By the use of the preponderance index described above in the electrocardiographic study of 1200 individuals, values of +20 and -15 have been found to be close to the border-line of normality (Tables I and II). Indices of +20 to +30 and of -15 to -18 have usually indicated left and right ventricular preponderance respectively and those beyond +30 and -18 have always indicated ventricular preponderance in our series. The highest values in normal people indicate, as a rule, unusual cardiac position; for instance, a fairly high positive value in a short, fat person really indicating a horizontal position rather than left preponderance and a fairly high negative value in a tall, long-chested individual indicating a

“vertical heart.” The respiratory test which by inspiration lowers the diaphragm and straightens the heart and by expiration acts in the opposite way is useful in the analysis of doubtful cases. Left ventricular preponderance in a short-chested person would give rise to an electrocardiogram of exaggerated left ventricular preponderance.

P deflections over 3×10^{-4} millivolts in amplitude or over 0.1 second in duration almost always indicate the presence of auricular hypertrophy (Table III).

TABLE I.—TABLE OF LEFT VENTRICULAR PREPONDERANCE.

Index of preponderance.	Total number of cases.	Aortic regurgitation.	Blood-pressure of 180 mm. or more without aortic regurgitation.	Aorta dilated or roughened without aortic regurgitation or hypertension.	Miscellaneous.
Above +30 . . .	21	9	12	0	
+20 to +30 inclusive	61	22	18	11	10 (8 normal)
Total	82	31	30	11	10

Respiratory test on 10 of first three groups; index of 8 stayed high. Index of 5 of last group became normal with respiratory test.

TABLE II.—TABLE OF RIGHT VENTRICULAR PREPONDERANCE.

Index of preponderance.	Total number of cases.	Mitral stenosis.	Rheumatic mitral disease without stenosis.	Pulmonary stenosis (congenital heart)	Chronic emphysema.	Normal.
Beyond -18 . . .	15	9	2	3	1	0
-15 to -18 inclusive	7	4	0	0	0	3
Total	22	13	2	3	1	3

TABLE III.—ENLARGED P DEFLECTION.

Over 3×10^{-4} volts in amplitude, or over 0.1 sec. wide, or both.

Total number of cases.	Mitral stenosis.	Rheumatic mitral disease without stenosis.	Hyperthyroidism.	Miscellaneous.	Right ventricular preponderance index of -15 or beyond.	Preponderance index minus.
20	11	5	1	1 with paroxysmal tachycardia. 1 with paroxysmal auricular fibrillation. 1 with syphilis.	11	19

One case with +17 had aortic stenosis as well as mitral stenosis.

CHOLESTEROHYDROTHORAX, OBSERVATIONS UPON A CASE.

BY B. F. WEEMS, JR., M.D.

NEW YORK CITY.

(From the Department of Medicine, Cornell Medical College Dispensary, and the Department of Clinical Pathology.)

THE problem of cholesterol metabolism commands a position of increasing interest to the medical profession today. Many striking facts about cholesterol have been collected through recent experimental studies, but a clear understanding of its role in human physiology has not yet been attained. For this reason it would seem important that all new or unusual data upon the subject be made matter of careful record.

The occurrence of a large quantity of cholesterol crystals in a pleural effusion is certainly a rare enough phenomenon to merit such attention. Since I observed this phenomenon several months ago I have been unable to discover a clinician or pathologist who remembers ever having seen or heard of such a case. This circumstance led me to a careful search of the medical literature, in which I have found astonishingly few observations of the kind recorded.

In 1908 Ruppert¹ reported a case of his own in which he had found cholesterol crystals in the pleural fluid. At that time he could find but two other similar cases in all the literature. After a thorough review of the medical literature since then I have been unable to add any other cases, although the subject of pleurisy, as well as that of cholesterol, has received particular attention.

In the various classifications of pleurisies made recently by French and German authors (Patein,² Chauffard,³ Méhu,⁴ Halipre,⁵ Müller,⁶ Schlesinger⁷ and many others), based upon thousands of analyses, there is no mention of the occurrence of free cholesterol. Patein in describing a rather rare type of pleural effusion, which he terms chyliform, states that in some of these small quantities of cholesterol had been recognized by chemical analysis. Also in the cases of true chylothorax, recently reviewed by Lewin,⁸ a small quantity of cholesterol was regularly encountered. But this alimentary cholesterol, coming directly from the lacteals of the mesentery, bears no relation to such deposits as the one here considered. Likewise in the analyses of over 300 pleural fluids, made in the Cornell labora-

¹ Münch. med. Wehnschr., 1908, lx, 510.

² Jour. de Pharm. et de Chem., 1915, (s. 7), xi, 265.

³ Presse Méd. (Paris), 1915, xxiii, 341.

⁴ Arch. Générale de Méd., September, 1881, ii, 257.

⁵ Presse Méd., August 19, 1905, 523.

⁶ Jour. de Méd. internat., 1906 (s. 221).

⁷ Ztschr. f. klin. Med. u. Kinderheilkund., 1914, xiii, 138 (bibliography).

⁸ AM. JOUR. MED. SC., 1916, clii, 71.

tory of clinical pathology, where one case of chylothorax is recorded, there is no mention of any case of cholesterohydrothorax.

The patient who furnished the data of this report appeared on February 17, 1916, in the Cornell medical dispensary.

CASE HISTORY.—Family History. William Delaney, aged fifty-one years, one of ten children, was born in Ireland of healthy parents. There is no record in his family of hereditary diseases nor of any metabolic disturbances, such as gout, diabetes, extreme obesity, nor of any other morbid peculiarities, such as prevalence of gall-stones, of early apoplexy, of goiter, gigantism or acromegaly.

Early History. He was "always healthy" throughout childhood, youth and early manhood, subject to no catarrhal diseases, and except for measles at the age of six or seven years was never sick in any way until thirteen years ago.

Marital. He is married, the father of five healthy children, one other having died in infancy, cause unknown.

Venereal. A questionable lesion on the penis twenty-three years ago; no subsequent luetic manifestations. Gonorrhœa twenty years ago; no sequelæ.

Occupation. Has worked steadily as a carpenter since boyhood.

Previous Illness. Thirteen years ago, in 1903, while engaged at work in a dusty, poorly ventilated tobacco factory his health began to fail. He recalls few symptoms. "Just kept going down hill." Coughed very rarely as he remembers, and complained of no definite pain. He continued working for two or three months, and when he finally consulted a doctor he was immediately sent to Bellevue Hospital. Here his left chest was aspirated and 94 ounces of fluid removed. The character of this fluid could not be definitely ascertained, as the record of his admission could not be found, but the patient asserts that it was quite clear and of a slightly yellowish tinge. He was very weak after the aspiration, but insisted upon going home the next day. A few days afterward he returned to work and kept hard at it in spite of his feeble condition. He felt "rocky and all played out," as he puts it, for a long time, but was determined to work it off. Apparently his condition did improve somewhat, for he did not have to stop working again until four years later, in 1907. At this time he had an attack of what he called "dry pleurisy." He cannot remember a distinct chill, but the attack came on suddenly, with a cough and pain in the left side. He had a high fever, was in bed five weeks, delirious part of the time and was attended upon several occasions by a private doctor.

Again, he went back to work in the early period of convalescence and worked hard without cessation up to the present time. His strength was greatly reduced, and very little exertion would make him short of breath. Occasionally he suffered pain in the chest, and every winter was tormented by a persistent cough.

Dietary Considerations. During the last seven or eight years, practically ever since the last severe illness, the patient has noticed that pork does not agree with him. It destroys his appetite for a number of days every time he eats it. The fat of beef is well borne, he declares, in respect to its effect upon appetite and digestion, but it always acts upon him as a cathartic. Eggs have likewise disagreed with him, in every form except as a single one added raw to a glass of milk. He relishes kidney stew but seldom indulges in it, and he cares little for fresh vegetables. His favorite food, and, indeed almost constant diet for many years, has been beefsteak and potatoes.

Habits. He always drank beer and ale in generous quantities, but little whisky until five or six years ago, when he began to use it steadily, often to the exclusion of food, and in gradually increasing amount. For a long time he drank three or four glasses a day. He believed it strengthened him for his work, consequently as his health failed more and more he increased it to six or eight glasses. Thus his tolerance became high. He was never "drunk," but kept steadily at work all this time.

Tobacco. He was an excessive pipe-smoker for many years, but a moderate smoker now.

Present Illness. On February 2, 1916, patient was forced to quit work, and on the 17th he applied at the dispensary. His dyspnea had steadily increased and was aggravated by a chronic cough, worse at night, productive of a moderate amount of tenacious, whitish sputum. He had had no hemoptysis, no chills or fever; his appetite had been getting poorer each day. Bowels were regular.

Physical Examination. A tall, scrawny man, aged fifty-one years, appearing older, quite gray already, somewhat stooped and decidedly emaciated, with suggestion of alcoholism in the facies, heightened by a considerable degree of congestion and cyanosis of the nose and other extremities. Height, 6 feet 2 inches; weight, 132 pounds. Breathing rapid and shallow: rate, 32. Temperature, 98.7° F. The skin shows only early senile changes. *Head:* normal brachycephalic calvarium. *Eyes:* moderately advanced arcus senilis, pupils unequal in size and irregular in outline, but react well to light and accommodation. *Teeth:* poorly preserved; gingivitis present. *Tongue:* slightly coated and tremulous. *Neck:* negative. *Thorax:* long and narrow, with limited expansion, more marked on left side. *Lungs:* the characteristic signs of left-sided pleural effusion. Behind the dulness extends to the midscapular region and to the side it coalesces with the left cardiac dulness. There is some harshness of breath sounds over the right upper lobe and scattered subcrepitant rales over both lungs. There is hyperresonance over the right lower lobe, the base of which extends to the level of the twelfth spine. *Heart:* area of cardiac dulness cannot be determined on the left; to the right it extends 3 cm. beyond the external margin

of the sternum. There is a soft systolic murmur at apex and base, not transmitted, and the first sound at the apex is short and relatively weak. *Pulse*: regular in rate and rhythm, of fair size, rather poorly sustained, no increased tension. *Blood-pressure*: systolic, 150; diastolic, 100. *Arteries*: thickened and extremely tortuous, the pulsations in brachials plainly visible. *Abdomen*: slightly convex, musculature, in good tone, no resistance about gall-bladder or elsewhere; no masses felt. The liver edge can neither be felt nor percussed beneath the costal margin. The first evidence of deep hepatic dulness, in sitting and reclining posture, is reached at the level of the sixth rib, in the right midclavicular line, actual flatness first at the seventh rib, one inch below the level of the tip of the xiphoid. The flatness can be traced downward a very short distance, a little over an inch. In the anterior axillary line the liver flatness begins at the ninth rib; in posterior axillary, at the tenth; behind, at the level of the twelfth spine. The first change of deep percussion is approximately one inch above this plane. The vertical extent of hepatic dulness, in the midaxillary line, is about two inches. *Spleen and kidneys*: not palpable. *Extremities and deep reflexes*: normal.

Radiograph of chest confirms the diagnosis of left-sided hydrothorax, and reveals, besides, a number of moderately dense, rather diffuse shadows in the upper right lobe, interpreted as tubercular in character, also a sharply defined, dense shadow, about the size of a hazel nut, in the left chest, on the level of the ninth rib, apparently a calcified node.

Sputum: negative for tuberculosis. *Urine*: normal amber color; specific gravity, 1020; faintest trace of albumin and very rare hyaline casts; no sugar. *Blood Wassermann*, negative.

On April 5, 1916, the left chest was aspirated. In the midst of the operation, certainly before more than two-thirds of the fluid had been withdrawn, dragging pain in the left chest became so severe and the pulse so weak that an abrupt termination was necessary. After aspiration the dulness was considerably diminished but still quite distinct as high up as the angle of the scapular behind and to the cardiac apex in front.

The singular appearance of this fluid excited immediate curiosity. It was yellowish gray in color, quite turbid, and peculiarly glistening in reflected light, filled with tiny, scale-like particles, which, upon the least agitation, circulated about, imparting a beautiful satin-like sheen to the surface of the fluid. The fluid was quite odorless, with a faintly salty taste. Upon standing the suspended particles sank promptly to the bottom and the volume of this gray sediment was almost as great as that of the now translucent supernatant fluid.

Microscopic examination, confirmed by the sulphuric acid color test and the qualitative reaction of Salkowski, identified the glittering scales as cholesterol crystals.

There were very few other formed elements present, a few large

cells, evidently of endothelial origin, and an occasional smaller cell, probably leukocytic. All of these cells showed abundant fatty granules, and there were many other such granules floating free in the fluid. No cells were encountered that did not show degenerative changes. No red corpuscles, nor shadows of such, could be found. No bacteria could be discovered by the usual staining methods, and aërobic cultures on broth and agar were negative.

The volume of the fluid was 1200 c.c.; specific gravity, 1023; albumin (Kjeldahl), 6.69 per cent. Total cholesterol (after saponification of esters), 1.39 per cent.⁹ Fatty acids, 33 per cent.¹⁰ Lecithin was present in very small amount, but not estimated.

The cholesterol of the blood was determined by Csonka's¹¹ modification, of the Autenrieth-Funk¹² colorimetric method. This was done on May 6. One cubic centimeter of the whole blood contained 2.5 mg. of cholesterol. Two days later blood was drawn, allowed to clot and the fresh serum pipetted off. This was found to contain 3 mg. per cubic centimeter. A serum of a normal individual, done at the same time as a control, contained but 0.7 mg.

A large quantity of urine was extracted with ether and tested by the same delicate method, but showed no trace of cholesterol.

Since the first paracentesis on April 5, 1916, two other aspirations have been performed. In the first of these, on April 18, the same severe pain and shock interrupted the operation very early in its course; but in the last, May 6, it was possible to withdraw all the fluid that would flow.

The second pleural fluid was not analyzed. The cholesterol crystals, still abundant, were not nearly in such proportion as at first.

The third fluid was still poorer in cholesterol. The crystals were smaller and many of them had lost their characteristic form and sharpness of outline. The relative proportion of fatty granules and fatty degenerated cells seemed to have increased. The fluid was less turbid but of a darker amber hue. Specific gravity, 1020; albumin (Kjeldahl), 3.85 per cent. Cultures of this fluid, on several media, by anaërobic as well as aërobic methods, were negative.

A considerable amount of pain about the heart and left pleura followed the aspirations, but at the same time there was a gratifying improvement in the patient's general condition, with abatement of cough, easier breathing, better appetite and increased strength.

Definite dulness and impairment of breath sounds at the base of the left lung persisted after the last aspiration, and was attributed

⁹ Measured quantity of material, saponified under reflux, with alcoholic KOH, neutralized, extracted with ether, dried residue extracted with petroleum ether, vacuum dried and weighed.

¹⁰ Method of Gephart and Csonka, *Jour. Biol. Chem.*, 1914, xix, 521.

¹¹ *Jour. Biol. Chem.*, 1916, xxiv, 431.

¹² *Münc. med. Wchnschr.*, 1913, No. 23, lx, 1, 1243.

to probable thickening of the pleura. These signs had not changed noticeably when the patient was seen a month later.

Two years ago Schlesinger made a very thorough study of the pleurisy of old age, and in his exhaustive article he emphasized the frequency with which advanced sclerotic changes are found in the pleural membranes of the arteriosclerotic and senile. Pic-Bonnamour¹³ emphasized the same point. A general thickening of the membranes, with spots and streaks which often attain cartilaginous consistency (*the plaques du frottement*, overlying the ribs), atrophy and obstruction of the blood and lymph vessels, as well as degeneration of the lymph glands at the hilum, are the significant changes noted. That these regressive changes are in large measure responsible for the diminished resorptive power of the membranes, and therefore for the frequent occurrence of long persistent effusions in the aged, is hardly to be questioned. Furthermore, it has been discovered that in the exudative pleurisy of old age hemorrhagic effusions are relatively frequent (Crepin), while, according to Schlesinger, seropurulent effusions are found in about 33 per cent. of all cases. This means that the disintegration of cellular exudates within sclerotic, pleural cavities is in nowise an uncommon process. But such disintegration necessarily results in the release of the cholesterol constituent of the cells. In fact, this cellular disintegration is the commonly accepted explanation of the cholesterol deposits found in old pus cavities, in tubercular masses and in old cysts. Yet common as is this process of chronic pleural effusion with cellular disintegration, deposits of cholesterol crystals are not often found. Evidently some other factor, which has not yet been recognized, is concerned in the production of this phenomenon. A brief consideration of the data of the other recorded cases might furnish some important suggestion upon this point.

The earliest case, reported by Churton¹⁴ in 1882, was that of an English laborer, aged thirty-eight years, who had suffered for several years with serous pleurisy and who died in the hospital, after numerous aspirations, with empyema. The pleural exudate, rich in cholesterol crystals (percentage not determined), contained also an abundance of red and white cells. There were no other significant facts recorded.

The second case was briefly mentioned in Rosenbach's treatise upon the diseases of the pleura in Nothnagel's *Handbuch*. In an autopsy upon a non-tuberculous woman he found a mass of cell detritus, blood pigment and cholesterol crystals in a ten-year-old encapsulated, pleural effusion. Neither age nor history of the patient was given.

The third case, reported by Ruppert in 1908, was that of a much depleted, alcoholic vagabond, who had had a pleural effusion twelve

¹³ Paris, 1912, O. Doin et fils, 904, p. 8°.

¹⁴ Tr. Clin. Soc. (London), 1882, xv, 19.

years previously, and upon date of examination was suffering with dyspnea on exertion and pain in the chest. This case was reported in much greater detail than the other two. Both the clinical and pathological findings, so far as they were noted, conformed closely with those of my case. The accompanying table will show the similarity of the exudates:

Case.	Amount, c.c.	Specific gravity.	Albumin (Kjeldahl), per cent.	Total cholesterin, per cent.	Faty acids, per cent.	Cultures.
Ruppert	1750	1025	6.60	1.29	0.36	Sterile.
Weems	1200	1023	6.69	1.39	0.33	Sterile.

Such close conformity as these two cases display would strongly bespeak an identical underlying condition, but examination of the data does not reveal what this condition is.

The histories of these 3 cases are so incomplete and the clinical observations so meager that no common factors can be discovered upon which a satisfactory explanatory hypothesis might rest. There certainly appears to be small likelihood of a purely anatomical pathological basis for the condition of cholesterohydrothorax. A much more likely basis would seem to be a peculiar disturbance of cholesterol metabolism. Although we may not discover the exact nature of this disturbance a review of the subject of cholesterol metabolism, with this purpose in mind, should be of decided interest and profit.

Almost without exception, in those conditions in which abnormal infiltrations or deposits of cholesterol occur, *e. g.*, pregnancy,¹⁵ diabetes,¹⁶ obesity,¹⁷ chronic nephritis, arteriosclerosis, eclampsia, jaundice and xanthelasma, a hypercholesterolemia has been found.^{18 19 20 21 22} Such habitual coincidence of two factors cannot but suggest a direct relationship between them. Other evidence in support of this suggestion is not far to seek. The figures of blood cholesterol determinations, made under a great variety of conditions, reveal the fact that the fluctuation of this substance in the blood is confined within comparatively narrow limits. The normal figure set down by Klinkert,¹⁸ later confirmed by Bacmeister and Henes,¹⁷ and now practically established, is 1.5 to 1.8 gm. per 1000. Figures under 1 and over 2 are considered abnormal. The highest figures reported by Klinkert are for chronic parenchymatous nephritis, 4.26; for

¹⁵ Hermann and Neumann: Wiener klin. Wehnschr., 1912, xxv, 1557.

¹⁶ Klemper and Umber: Ztschr. f. klin. Med., Berlin, 1907, lxi, 145; 1908, lxxv, 340.

¹⁷ Bacmeister and Henes: Deutsch. med. Wehnschr., 1913, xxix, 1, 544.

¹⁸ Berl. klin. Wehnschr., 1913, l, 1, 820.

¹⁹ Fischer: Virchows Arch., 1903, clxxii, 20 and 218.

²⁰ Weston and Kent: Jour. Med. Research, Boston, 1912, xxvi, 47 and 531.

²¹ Grigaut: Various arts. in Compt. rend. and Semaine Médical.

²² Iscovesco: Compt. rend. Soc. biol., Paris, 1912, lxxii, 225.

diabetes with marked acidosis, 4.965; for pregnancy, 4.25. In spite of conditions most favorable to the accumulation of large quantities of blood cholesterol, such, for example, as complete biliary obstruction, the high-level mark of 5 gm. per liter of serum is very rarely attained; while it is very commonly observed long before this unusual concentration is reached, that abnormal infiltrations of cholesterol have already appeared in various tissues of the body. Thus, xanthelasma, a cholesterol-ester infiltration of certain cells in the skin, frequently appears during the hypercholesterolemia of pregnancy, to disappear gradually as the blood cholesterol sinks to the normal. The same holds true for the retinal white spots²³ (cholesterol-ester) in eclampsia, in chronic nephritis and in diabetes mellitus. Moreover, Windhaus²⁴ has shown us to what an enormous extent cholesterol deposition takes place in the walls of the arteries during the progress of atherosclerosis, with which a hypercholesterolemia is always associated.

Experimental evidence of this nature was first adduced by the Russian investigators. Anitschow²⁵ showed that rabbits fed upon a cholesterol-rich diet develop a condition of the arteries quite analogous to human arteriosclerosis, with similar deposition of cholesterol in the vessel walls. Dogs who normally possess a greater power of metabolizing and eliminating cholesterol could not be so affected. By feeding rabbits pure cholesterol, Anitschow and Chalатов²⁶ rapidly raised the cholesterol level of their bloods and produced a cholesterol infiltration of nearly all the organs of their bodies.

The increase of cholesterol-ester in the adrenals, when the blood cholesterol is increased, a fact carefully studied and demonstrated experimentally by a great number of observers (Hueck,²⁷ Knack,²⁸ Wacker and Hueck,²⁹ Sternberg,³⁰ Borberg,³¹ and others), has never been satisfactorily explained, but seems to stand largely upon the same basis as the phenomena produced by Anitschow.

Hoesli³² produced in rabbits with hypercholesterolemia a skin lesion closely related to xanthelasma, in which the young fibroblasts became laden with cholesterol and cholesterol-ester. But nothing of the nature of xanthomatuberosum could be produced. Weil,³³ in a study of the significance of giant-cell tumors of the tendons and joints, found the uniform presence of hypercholesterolemia. He concluded that there is no essential difference between xanthoma of the skin and the tumors in question. Both, he believes, represent

²³ Lauber and Adamuk: Arch. f. Opth., Leipsig, 1909, lxxix, 429.

²⁴ Ztschr. f. physiol. Chem., Strassburg, 1910, lxxvii, 174.

²⁵ Ziegler's Beitr., 1913, lvi, 379; Deutsch. med. Wchnschr., 1913, xxxix, 741.

²⁶ Centralbl. f. allg. Path. u. path. Anat., 1913, xxiv, 1.

²⁷ Verhandl. d. Deutsch. path. Gesellsch., Jena, 1914, xvii, 149-156.

²⁸ Virchows Arch., 1915, cexx, 36 (bibliography).

²⁹ Arch. f. exp. Path. u. Pharm., 1914, lxxviii, 432.

³⁰ Beitr. z. path. Anat. u. z. allg. Path., 1915, lx, 91; *ibid.*, 1914, lx, 114.

³¹ Skandin. Arch. f. Physiol., Leipsig, 1914, xxxii, 15-287.

³² Brun's Beitr., 1914, xcv, 198.

³³ Berl. klin. Wchnschr., 1915 (No. 6), 129.

infiltration processes on the basis of a general disturbance of cholesterol metabolism in which the one presents a mild tissue reaction and the other an energetic reaction.

The experimental facts strongly support the view that the various mentioned forms of tissue infiltration serve, to a large extent at least, as channels of vicarious elimination of cholesterol, when that substance reaches an intolerable concentration in the blood. The exact mechanism of this tissue infiltration, especially in the human cases, is a question of the greatest interest and importance, but one upon which, up to the present time, very little light has been thrown. The presumption is strong, however, that some other factor besides the high concentration of blood cholesterol is involved in the production of the phenomenon. The deposition of cholesterol-esters seems closely analogous to the production of gouty tophi. That the deposition is preceded in both cases by a toxic injury to the cells is certainly a probable hypothesis. That such injury and deposition may occur without hypercholesterolemia is suggested by the report of Rosenbloom,³⁴ who was unable to find hypercholesterolemia in a pronounced case of xanthoma multiplex. By both the clinical and experimental facts, however, it seems firmly enough established that the blood cholesterol cannot be pushed beyond a certain level without provoking, somewhere in the body, a tissue deposition or infiltration.

The fact that with the dog, accustomed as this animal is to a cholesterol-rich diet, feeding experiments failed to produce cholesterol infiltration of the tissues or even to raise, to any appreciable extent, the level of the blood cholesterol, while both these phenomena could readily be achieved with rabbits, led to the tacit assumption that the difference was due to the greater deesterizing power in the liver of the dog. But this unwarranted assumption is contradicted by the only direct experimental testimony so far presented. D'Amato,³⁵ feeding large quantities of lipoids to dogs and measuring the cholesterol of the bile, found that only a small fraction of the excess was thus excreted. The rest, he was forced to conclude, was otherwise disposed of in the organism. Comparing D'Amato's discovery with the common clinical observation that in pregnancy, although the cholesterol content of the diet may be unchanged and basal metabolism lowered, there is, nevertheless, an increase in the cholesterol content of both the bile and the blood, we are led to conclude that the animal organism possesses the power of converting into some other form a greater or less quantity of cholesterol, and that this function is considerably less in the pregnant than in the non-pregnant state. It is interesting to note that up to the present time the most widely accepted theories of cholesterol metabolism have not accepted this conclusion.

³⁴ Arch. Int. Med., October, 1913, xii, 395.

³⁵ Biochem. Ztschr. (Berlin), 1915, lxix, 217.

In an extensive series of researches upon the chemistry and metabolism of cholesterol, Lifschütz³⁶ has disclosed some strongly presumptive evidence in support of the theory that the nitrogen and sulphur-free constituent of the bile acid salts is derived quantitatively from cholesterol. He presents good grounds, moreover, for the belief that the first step in the process consists in the conversion of cholesterol into oxysterol. This latter substance he has identified in most of the tissues of the body. He looks upon this preliminary oxidation of cholesterol as a purely chemical reaction, taking place for the most part in the blood stream. He has demonstrated the reaction in mixtures of oxyhemoglobin and cholesterol dissolved in acetic acid, and has further shown that the power of these hemoglobin solutions to oxidize cholesterol is greatly reduced, if not entirely inhibited, by the presence of more readily oxidizable substances such as the lower alcohols. In spite of the original and painstaking character of Lifschütz's work and the vital nature of its evidence it seems to have been largely ignored by the numerous other investigators of the physiological chemistry of cholesterol.

Just what becomes of a deposit of cholesterol in the tissues has been the subject of considerable curiosity. Basten³⁷ found that cholesterol injected under the skin of rabbits causes prompt necrosis, followed rapidly by granulation tissue and the appearance of large cells, which take up the crystals in the form of cholesterol-esters. Corpor³⁸ carried out the same experiment in guinea-pigs, finding that the deposit gradually disappears. Klotz and Bothwell³⁹ injected a mixture of cholesterol and oil into the veins of rabbits, producing obstructive lesions in the lungs, in which phagocytic cells eventually appeared ingesting the oil and cholesterol, in the form of tiny globules, of which some were anisotropic, *i. e.*, cholesterol-esters. That the initial step in the removal of cholesterol from the tissues is represented by its ingestion by giant cells in the changed form of cholesterol-esters has been repeatedly demonstrated. What next becomes of this cholesterol-ester, investigation has not positively determined. The assumption is well-nigh universal, however, that as ester or in uncombined form it finds its way eventually into the blood stream. But there is no convincing proof that chemical change does not occur within the cells. That such change might be controlled by intracellular oxidases is a speculation that cannot be lightly discarded. The demonstration of oxysterol in the various tissues by Lifschütz is to be considered in this relation.

Once incorporated in the blood stream all authorities agree that a part of the cholesterol is eliminated by the liver and excreted in the

³⁶ Frequent Articles from 1907 to 1914 in *Ztschr. f. phys. Chem. and Biochem. Ztschr.*

³⁷ *Virchows Arch.*, 1915, cccx, 126.

³⁸ *Jour. Biol. Chem.*, 1912, xi, 37; *Jour. Exp. Med.*, 1915, xxi, 179.

³⁹ *Proc. Soc. Exp. Biol. and Med.*, 1915, xii, xciv, 159.

bile; another part, it is as generally agreed, is utilized as an indispensable constituent in the manufacture of new cells; but the theory that a third part, and quite a considerable proportion, is oxidized in the blood stream and converted (probably by the liver) into the N- and S-free constituent of the bile acids seems at present to enjoy the support of a single authority.

It is the writer's opinion that future investigation will establish the theory that the N- and S-free constituent of the bile acids is derived from the oxidation of cholesterol and that the oxidation takes place, not as a simple chemical reaction, as supposed by Lifschütz, but under the regulation of a ferment (perhaps a product of internal secretion) in the same way as the other special oxidative processes of the body, disturbances of which are exemplified in hypothyroidism and pregnancy. The case herein reported lends some support to this view. Its various features are not readily explicable upon the basis of any other theory yet advanced. The inability to digest any considerable quantity of fat, in association with an unusually small liver, naturally suggests a deficient liver function, specifically a deficient secretion of bile salts. It is quite conceivable that the long and excessive use of alcohol (alone or in connection with some other factor) might serve to impair the cholesterol-oxidizing-ferment or to divert it from its normal function, thus diminishing the production of the N- and S-free constituent of the bile acids. However effected, any reduction of cholesterol oxidation would presumably result in an increase of that substance in the blood, a result which could only be enhanced by the heavy intake of the meat-rich diet upon which my patient chiefly subsisted. With the constant cholesterol saturation of the blood thus produced it seems to some extent reasonable that the accumulation in the pleural exudate could not be absorbed.

This tentative explanation is presented for whatever suggestive value it may possess, with the hope that it may stimulate a keener interest in a subject which is rapidly acquiring greater clinical significance.

THE CHEMOTHERAPY OF LEPROSY AND TUBERCULOSIS.

BY T. SUGAI, M.D.,

OSAKA, JAPAN.

INTRODUCTION. Robert Koch, in 1890, stated that auricyanide is toxic for tubercle bacilli, although it has no effect on animals not infected with tubercle bacilli. Bruck and Gluck stated, in 1913, that potassium auricyanide is efficacious for lupus. Von Linden and Meissen employed the iodomethylene blue and copper lecithin compounds, both intramuscularly and cutaneously, in the treat-

ment of tuberculosis patients, and succeeded in establishing certain favorable results (1913). Strauss obtained good results with the use of iodomethylene blue and copper potassium tartrate injected intravenously and also applied cutaneously (1913). Bodmer recommended copper lecithin, especially in combination with tuberculin. Demark recognized the value of injections of electrocuprol. The effect of copper salvarsan on persons suffering from tuberculosis and leprosy was investigated by Shiga, in 1915, with certain good results. Favorable results were also obtained by Koga, in 1915, with potassium cuprocyanide, prepared by himself and tested on tuberculous men and animals.

The writer has undertaken an investigation of the chemotherapy of leprosy and tuberculosis, with the results here set forth.

Agent and Form of Application. The agent, which I have called potassium cuprocyanide, is a combination of 2 parts of potassium cyanide and 1 part of cuprous cyanide, and is in the form of small white, needle-shaped crystals, which are soluble in water and alcohol. Five mg. per kilogram of body weight is the lethal dose for the rabbit.

Dose. The patient received an injection of a 0.1 to 1 per cent. of the aqueous solution every ten days, the amount injected being equivalent to 0.25 to 0.3 mg. per kilogram of body weight.

RESULTS OF TREATMENT IN LEPROSY. One to three injections of the agent produce the following effects in leprosy patients:

The nodes gradually become soft, or begin to bleed, after which they diminish in size or are resorbed, in time completely disappearing. The leprosy ulcers heal and form scars only after two or three injections. They lose their characteristic color eventually. Sensory disturbances are also overcome when the swollen nerves have had time to shrink to their normal size. The treatment frequently has the effect of stimulating the growth of hair in areas where it has fallen out. A summary of the results of the use of the agent in leprosy is as follows:

AFTER 1 TO 3 INJECTIONS (TO JUNE 5, 1915).

	Cases.
Diminution or disappearance of nodes	17
Drying up, cicatrization or healing of ulcers	2
Improvement of vision	2
Temporary increase in size of nodes	4
No change in symptoms	11
	—
Total	36

Continued injections often produced remarkable effects. Injections given in the case of other forms of leprosy were also productive of good results.

Histological Changes in the Diminished Nodes as a Result of Several Injections. Necrotic, cheesy foci appeared here and there in the nodes, at the peripheries of which were many giant cells containing several nuclei. The leprosy bacilli had collected in places; often

they had disintegrated into granular masses or had formed a diffuse and homogeneous swelling. They were usually greatly reduced in number.

TABLE I.—ANATOMICAL FINDINGS IN ANIMALS.

No. of animal.	Lymph glands.	Fatty tissue of peritoneum.	Liver.	Lung.	Result.
1	+	+	+	-	Slight change.
2	+	..	+	+	Slight change.
3	..	+	..	+	Marked change.
4	+	..	-	-	Very slight change.
5	+	..	++	++	Marked change.
control					

TABLE II.

No. of guinea-pig.	Body weight.	Date of injection of tubercle bacilli.	Date of injection and dose of solution.		Death.
			First time.	Second time.	
A	95 gr.	1 mg. May 26	June 6 0.05	June 10; accidental.
B	105 "	May 26	June 6 0.05	June 10; accidental.
C	95 "	May 26	June 6 0.05	June 10; accidental.
D	95 "	May 26	June 6 0.05	June 8; died.
E	125 "	May 26	May 26 0.05	June 6 0.05	June 10; accidental.
F	130 "	May 26	May 26 0.05	June 6 0.05	June 10; accidental.
G	100 "	May 26	Control	June 10; accidental.
H	105 "	May 26	Control	June 10; accidental.
I	105 "	May 26	Control	June 10; accidental.
K	110 "	May 26	Control	June 7; died.
L	120 "	May 26	Control	June 9; died.

TABLE III.

No. of animal.	Macroscopic findings.				Microscopic findings and number of bacilli.					Result.
	Fatty tissue of peritoneum.	Spleen.	Liver.	Lung.	Lymph gland.	Fatty tissue of peritoneum.	Spleen.	Liver.	Lung.	
A	++	+	++	-	+	++	++
C	+++	+	+	-	-	+	..	+	-	++
D	+++	+	-	++	?	++
E	+++	++	+	+	..	++	+	++	?	++
F	+++	++	?	?	-	+ No bacilli	..	+ No bacilli	..	++
G	+++	++	+	+	++	+++	..	++	..	+++
Control K	+++	?	+	+	+	+++	-	+++	+	+++
Control L	+++	++	+++	+++	..	++	..	++	+	+++
Control										

ANIMAL EXPERIMENTATION WITH THE THERAPEUTIC AGENT IN TUBERCULOSIS. *Series I.* Tubercle bacilli were injected in doses

TABLE IV.—SERIES III.

No. of guinea-pig.	Body weight.	Date of injection of tubercle bacilli. 1 mg.	Dose of injection, 0.1% solution.								Body weight.			Deaths.
			June 11	July 19	July 26	Aug. 6	Aug. 16	Aug. 27	Sept. 7	Sept. 17	July 13	July 26	Sept. 17	
1	335	June 11	0.5	0.15	0.2	0.15	0.15	0.12	0.1	0.1	340	345	390	June 20; killed. Weight 400.
2	210	"	0.5	0.1	0.2	275	260	..	July 30; died.
3	360	"	0.5	0.5	0.2	0.15	0.15	0.1	0.1	0.1	315	315	315	September 20; killed. Weight 245 (scabies).
4	395	"	390	370	..	August 6; died. Weight 300.
Control														

The tubercle bacilli were injected intraperitoneally and the agent intravenously.

of 1 mg. into the livers of five rabbits and followed by the intravenous injection of 2 to 4 cm. of a 0.1 per cent. aqueous solution of potassium cuprocyanide. One rabbit which did not receive the injection was retained as a control. The animals were killed and examined on the twenty-third day after injection.

The simultaneous injection of the agent and of the tubercle bacilli seems to produce an inhibition in the distribution and an increase of the tubercle bacilli.

Series II. The tubercle bacilli were injected intraperitoneally and the therapeutic solution intravenously. This series of animals was attacked and strangled by weasels on the evening of June 10. The next morning five animals (A, C, E, F and G) were found in a condition which made examination impossible. Animals B, H and I were lost.

TABLE V.—POSTMORTEM EXAMINATION.

No. of animal	Macroscopic findings.					Microscopic findings and number of bacilli.					Result.
	Fatty tissue of peritoneum.	Spleen.	Liver.	Lung.	Lymph gland.	Fatty tissue of peritoneum.	Spleen.	Liver.	Lung.	Lymph gland.	
1	-	-	-	-	-	-	-	-
2	..	+	+	-	+	..	+ bacilli ?	+ bacilli ?	+	+	+
3	-	-	-	+	-	..	+	+ No bacilli	-	+	+
4	+	++	++	++	+	++	++	..	++

The attempt shows a good effect in tuberculosis. The disease was finally arrested.

Result of Animal Experiments. If a sufficiently large number of tubercle bacilli be injected intraperitoneally into guinea-pigs the animals sicken and succumb in from five to seven weeks. But if the agent is afterward injected intravenously the animals live for a longer time or recover completely. Histological examination of the animals shows that the former tuberculous foci have healed and that the bacilli have entirely disappeared, while the control animals suffer the ordinary pathological tuberculous changes and finally die.

When the injection of tubercle bacilli into the liver of the rabbit is soon after followed by an intravenous injection of the agent an examination after twenty days will show that the spread of the tuberculous foci has become circumscribed and that the bacilli have diminished in number. When tubercle bacilli are injected intraperitoneally into guinea-pigs and the agent injected intravenously soon afterward the animal dies, as a rule, a few hours later, with chills and a high temperature. Under these conditions the tubercle bacilli which are present in the peritoneal fluids are usually found to have decomposed and become granular in character, whereas those found in the body cells have remained unchanged.

TABLE VI.—SERIES IV.

No. of guinea-pig.	Date of bacilli injection.	Body weight.	Dose of injection of 0.1 per cent. solution.						Body weight.			Death.	Remarks.	
			Aug. 6	Aug. 16	Aug. 27	Sept. 10	Sept. 17	Aug. 16	Aug. 27	Sept. 7	Sept. 17			
A	July 30	310	0.15	0.15	0.12	335	290	Aug. 31; died.	
B	July 30	370	0.15	0.15	0.12	0.1	..	405	400	370	Sept. 13; killed	Suffering from scabies.
C	July 30	375	0.15	0.15	0.12	0.1	0.1	405	400	380	340	..	Sept. 23; died.	Suffering severely from scabies.
D	July 30	280	0.15	0.15	0.12	0.1	0.1	390	450	516	560	October 1, weight 590 grams.
E	July 30	260	0.15	0.15	0.12	0.1	..	295	295	285	Sept. 13; killed	Suffering from scabies.
F	July 30	300	1	325	300	Aug. 31; died	
Control G	July 30	270	1	250	Aug. 16; died	
Control H	July 30	260	1	260	Aug. 21; died	

Both tubercle bacilli and agent were injected intravenously. The quantity of bacilli was 1 mg. per animal.

TABLE VII.—AUTOPSY EXAMINATIONS.

No. of animal.	Macroscopic findings.					Microscopic findings and number of bacilli.					Result.	Remarks.	
	Lymph gland.	Fatty tissue of peritonum.	Spleen.	Liver.	Lung.	Lymph gland.	Fatty tissue of peritonum.	Spleen.	Liver.	Lung.			
A	-	-	-	-	++	+	...	+	+	+	+	+	Bacilli in very small numbers.
B	-	...	-	-	++	+	...	++	++	++	+	+	
C	-	...	?	+	-	+	+	+	+	+	Bacilli in very small numbers. Quite well.
D	
E	-	-	-	-	+	+	++	+	+	Rather many bacilli in lungs. Few elsewhere.
F	++	-	++	++	++	++	++	++	++	
Control	++	++	-	-	++	+	++	++	++	++	
Control	+	++	-	+	++	+	++	+	++	+	+	

This experiment demonstrates that the agent is efficacious in tuberculosis, finally effecting a cure.

Histological Findings. The tuberculous nodule is enveloped in a thick capsule, resembling connective tissue. The capsule sends out into the nodule numerous bundles of connective tissue, within which may be seen numerous lymph channels; this is undoubtedly a symptom of the resorption of the nodule. The bacilli in the nodule are often taken up by the epithelioid cells of the tissue and undergo morphological changes.



FIG. 1.—Lepra tuberculosa. Yamagata, aged thirty-three years. Before the injection. Date of photograph, May 13, 1915.



FIG. 2.—Same as Fig. 1 after the injection. Date of photograph, October 4, 1915.

RESULTS OF TREATMENT IN TUBERCULOSIS PATIENTS. A few days after the injection the lung symptoms become aggravated, the quantity of sputum raised is increased, a rise of temperature of about 1° frequently occurs and in many cases the patient feels weak and tired for from two to four days. Then conditions usually show marked improvement, the temperature falling gradually and the appetite being restored.

For three to six days after injection, hemorrhages may be frequent. The sputum is greatly reduced in quantity, even in severe cases, but frequently contains large numbers of bacilli for a long period. According to my experience the bacilli do not wholly disappear from

the sputum until ten to twenty injections have been administered. Patients in the first and second stages of the disease often feel well after five to ten injections. In such cases it is difficult to find the bacilli.



FIG. 3.—Lepra tuberculosa. Tsuchida, aged forty-three years. Before the injection. Date of photograph, May 13, 1915.

FIG. 4.—Same as Fig. 3 after the injection. Date of photograph, October 4, 1915.

Of the numerous cases of tuberculosis treated the results in 51 cases are tabulated below: Of these, 15 were in the first stage (apical catarrh), 28 in the second stage (infiltration) and 8 in the third stage (formation of cavities).

	Cases.
Marked improvement	5
Moderate improvement	19
Slight improvement	9
No improvement or aggravation of certain symptoms and improvement of others	6
Uncertain	11
Exacerbation	1
	<hr style="width: 10%; margin-left: auto; margin-right: 0;"/>
Total	51

A certain proportion of favorable results were also obtained in the case of other forms of tuberculosis.

Unfavorable Effects. In from 2 to 4 per cent. of patients there were chills and a rise of temperature several hours after injection. These symptoms continued for several hours and must undoubtedly be attributed to the inferior quality of the agent used in the particular cases or to an impure solution. In cases complicated with beriberi the agent may have an unfavorable effect. My limited experience, however, does not permit of any definite statement on this point.



FIG. 5.—*Lepra tuberculosa*. Nagai, aged fifty-one years. Before the injection. Date of photograph, May 13, 1915.



FIG. 6.—Same as Fig. 5 after the injection. Date of photograph, October 4, 1915.

SUMMARY. 1. Potassium cuprocyanide when injected intravenously has an extremely beneficial effect in leprosy. It is probable that a cure might be effected if the treatment were continued for from six months to a year.

2. A completely therapeutic effect in tuberculosis in animals has been demonstrated. The animals which received intravenous injections of potassium cuprocyanide lived longer than those which had no treatment. After eight to ten injections the animals were completely cured.

3. Potassium cuprocyanide obviously had a favorable effect on tuberculosis in man, including the pulmonary form.

STATUS LYMPHATICUS.

BY DOUGLAS SYMMERS, M.D.,

PROFESSOR OF PATHOLOGY IN THE UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL
COLLEGE, ACTING DIRECTOR OF LABORATORIES, BELLEVUE AND ALLIED
HOSPITALS.

(From the Pathological Laboratories of Bellevue and Allied Hospitals.)

THE association of sudden death with enlargement of the thymus gland was noted by Bichat early in the eighteenth century, but it remained for Paltauf and others of the Vienna school to show that persistence of the thymus in these circumstances is but one of a combination of hereditary anatomical imperfections occurring in the same body, constituting the condition which is now universally known under the somewhat ponderous and withal inadequate designation of status thymicolymphaticus, or, more simply, as status lymphaticus. Commencing in 1905, Dr. Charles Norris, some time director of laboratories at Bellevue Hospital, made a series of observations on certain peculiarities of configuration in status lymphaticus and called attention to their importance in the clinical detection of the condition. In addition, he pointed out the frequent association of status lymphaticus and certain lesions of the ductless glands, including exophthalmic goitre, Addison's disease, acromegaly and the like, together with its occurrence in suicides and others of unstable emotional qualities. In 1909 Dr. Norris addressed a letter to Professor Edmund von Neusser, of Vienna, directing his attention to the peculiarities of configuration by which status lymphaticus is characterized. Two years later von Neusser published a paper on "The Diagnosis of Status Lymphaticus,"¹ in which he made graceful acknowledgment of his indebtedness to Norris for the diagnostic criteria upon which his paper was founded. In the meantime Norris had read a paper on the same subject before the American Association of Pathologists and Bacteriologists, in Boston, in 1909, in which he made his observations a matter of public knowledge, and in the same year his paper was abstracted at length and published in Volume III of Johnson's *Surgical Diagnosis*.² In view of these facts it seems that, in simple fairness, the credit for establishing the clinical signs of status lymphaticus should be bestowed not upon the continental clinician but upon the American pathologist whose astute observations first brought them

¹ von Neusser: *Ausgewählte d. klin. Symptomat. u. Diag.*, Wien, 1911, p. 197.

² Johnson: *Surgical Diagnosis*, New York, 1910, iii, 704. This volume, although published under the imprint of 1910, was really released in 1909, the copy on file at the New York Academy of Medicine bearing the date of receipt of November 17, 1909.

to light in company with other facts of importance in the same connection, who, frankly and in good faith, submitted them for criticism by a former teacher, and was rewarded by having them incorporated in a paper which has since become a celebrated document in the archives of clinical medicine.

DEFINITION OF STATUS LYMPHATICUS. Status lymphaticus may be defined as a combination of hereditary constitutional anomalies, entering into which are certain peculiarities of configuration, with preservation or even hyperplasia of the thymus gland at an age when involution is to be expected, hyperplasia of the lymphoid cells in the lymph nodes, spleen, intestine and elsewhere, hypoplasia of the cardiovascular system, developmental deficiencies in the genitalia, and, incidentally, visceral defects of uncertain occurrence and irregular distribution. The condition sometimes is terminated by sudden death, usually in children, but occasionally in young adults.

Status lymphaticus as such is compatible with life; in fact, many subjects not only attain maturity but survive those involutinal changes in the lymphoid tissues which, when completed, deprive the condition of certain of its dangers. It is nevertheless a menace, and for at least two reasons: (1) Because it is attended by instability of the lymphoid tissues, providing a mechanism which, when it is once set in motion, is capable of so sensitizing the body as to produce anaphylactic phenomena varying in intensity from simple same irritability of the lymphoid tissues is apparently responsible urticarial rashes to convulsive seizures or sudden death. The for lowering the threshold of infection, particularly those infections which gain entrance through the pharyngeal and faucial tonsils and the intestinal tract. (2) It is a menace because it is attended by defective development of the muscular coat of the arteries, thus rendering them incapable of withstanding changes in blood-pressure which, in ordinary circumstances, are lightly borne.

CLINICAL ASPECTS OF STATUS LYMPHATICUS. Clinical interest in status lymphaticus seems to be focussed almost exclusively on the fact that life may be terminated abruptly on apparently trivial provocation. As a matter of truth, sudden death in status lymphaticus is a tragedy comparatively rarely enacted, but when it does occur the astonishing rapidity of the blow and the unexpected circumstances in which it is delivered are exceedingly impressive. In addition, status lymphaticus touches certain clinical problems of practical value which, however, appear to have been almost completely submerged in the contemplation of spectacular death. It will be the purpose of this paper not so much to emphasize the occurrence of sudden death in status lymphaticus as to impress still further the signs by which the condition may be detected in the living patient, the suggestive frequency with which it is asso-

ciated with various acute infections, with certain disturbances of the nervous system and of the ductless glands, with the occurrence of cerebral hemorrhage in the young, and, finally, its participation in the pathology of caisson disease.

CLINICAL SIGNS.—In the clinical conglomerate of scrofula the elder Gross long ago recognized the angelic child, in whom he pointed out the existence of a so-called lymphatic constitution and postulated a connection between it and an unusual susceptibility to tuberculosis, particularly of the bones, joints and lymph nodes. It is now known that children of this type are of the category of status lymphaticus. The angelic child may be described as delicately molded but beautifully proportioned, blue eyed or brown, with long lashes, finely chiselled features, transparent cheeks and rapid mutations in coloring, thin lips, smooth skin and silk-like hair, shapely limbs and quick, graceful movements, narrow waisted, mentally alert, often precocious—a thing of beauty, but lacking in the full promise of life. Such children are not even reasonably assured of maturity but are liable to be eliminated by sudden death or by tuberculosis, cerebrospinal meningitis or other infection. Still other children, with the stigmata of status lymphaticus, are physically and mentally sluggish, coarse featured and sometimes rachitic, but even in these the skin may be fine and the limbs shapely.

After puberty the clinical recognition of subjects of status lymphaticus is even more easily accomplished. In addition to the delicate texture of the skin, which may be velvety to the touch, dead white or faintly cream-colored, sometimes lusterless or paste-like, but rarely muddy, at other times swept by a faint sheen, and the well-nourished, often muscular, finely proportioned body, with its gracefully outlined arms, rotund and arching thighs and slender waist, it is found that in the male the pubic hairs assume the distribution of the female—that is to say, they are sharply defined in a transverse direction and do not tend to grow toward the umbilicus, while the penis is often small and the glans acorn-shaped. The facial and axillary hairs are scantily developed and the thoracic hairs are few in number or totally absent. An exception to this statement, however, is to be noted in certain subjects of status lymphaticus born along the shores of the Mediterranean, in whom the growth of hair may be abundant on both the face and trunk and of normal distribution, and in Orientals, many of whom, according to Crowell,³ are normally bereft of beard, mustache, axillary and thoracic hair as well as of hair on the extremities. In the female the recognition of status lymphaticus by inspection of the body is rather more difficult, but the diagnosis may be made with relative assurance by the

³ Phillipine Jour. Science, 1913, No. 2, viii, 77

unusually delicate texture of the skin, by accentuation of the graceful outlines of the body and by the presence of small axillary pads with the scanty growth of hair upon them. In very young children the presence of enlarged tonsils, adenoid vegetations in the nasopharynx and increase in the size and number of the follicles at the base of the tongue may or may not deserve attention as contributing factors in the diagnosis. The converse is imperative, however, that the diagnosis of status lymphaticus be made in those children in whom surgical removal of adenoids is contemplated. In children who have reached or passed the age of puberty, preservation of these enlarged lymphoid structures, together with palpable cervical and other superficial lymph nodes, assumes a place of slightly more significance, but, even at best, it is not a great aid to diagnosis, which, in most instances, may be established without taking these factors into consideration at all.

As age advances the configuration of the body in status lymphaticus may change, partly on account of muscular attrition, but largely because of alterations in the subcutaneous fat. As a rule, however, the conformation is retained to an extent sufficient to combine with the other external features to facilitate diagnosis, and even profound emaciation does not of necessity interfere.

INCIDENCE OF STATUS LYMPHATICUS. In Bellevue Hospital, in the past twelve years, 457 cases of status lymphaticus were encountered among 5652 autopsies (8 per cent.). In the first 4000 autopsies there were 249 cases. These have been analyzed, statistically and otherwise, and form the basis of this paper.

Sex.—Status lymphaticus was encountered 212 times in males and 37 times in females, which is in the proportion of about 6 to 1.

Age.

Under 1 year	22
1 to 10 years	10
11 to 20	"	20
21 to 30	"	62
31 to 40	"	57
41 to 50	"	41
51 to 60	"	19
Over 60	"	11

Race.—Of the 249 cases 25 occurred in negroes. In this race status lymphaticus, more commonly than in the white, is associated with a degree of muscular development which often is magnificent, the individual muscles standing out as streaming ridges beneath a skin almost as smooth as porcelain.

Of the 224 whites there were 40 Irish, 45 Germans, 7 Hungarians, 20 Italians, 5 Russians, 12 Poles, 3 French, 32 Swedes and 7 Syrians, and 52 in whom the nationality was not recorded. Crowell⁴ has

⁴ Loc cit.

encountered status lymphaticus among the Philipinos and other Orientals, and Whitmore⁵ among the races of British India, so that its geographical distribution is wide.

PATHOLOGY. The anatomical variations in status lymphaticus include of course those external features of configuration and development which have been enumerated, but, in addition, there are changes in other parts that are of importance. These may be classified and described accordingly as they involve (a) the lymphoid tissues, (b) the cardiovascular apparatus, (c) the genitalia and (d) under the heading of incidental anomalies of development.

Anatomical Types. In our autopsy protocols we are accustomed to describe two anatomical types depending upon the condition of the lymphoid tissues—status lymphaticus and recessive status lymphaticus. The former is associated with unusually well-developed changes in the lymphoid tissues and occurs at an age when these tissues are naturally flourishing. The recessive type is marked by atrophic changes in the lymphoid structures, varying in extent according to the time of involution, the configuration remaining the same except insofar as it may be modified by the waste of disease or age. Of the 249 cases there were 118 instances of status lymphaticus, 89 cases of recessive status lymphaticus and 42 cases in which the lymphoid tissues were in places hyperplastic, in other places atrophic, in other words, border-line examples, which, however, were tending in the direction of regression.

(a) **THE LYMPHOID TISSUES.** Of the 118 cases of well-developed status lymphaticus the thymus gland was hyperplastic in every instance. The weight of the gland was recorded in 66 cases. The youngest subject was a child of eight hours whose thymus weighed 70 grams and in whom death occurred suddenly, the oldest was an acromegalic individual, aged thirty-eight years, in whom the thymus also weighed 70 grams and in whom death was due to an intercurrent affection. The average weight of the thymus gland, grouped according to years, is shown in the following table:

Age.	Average weight, grams.	Number of cases.
Under 1 year	25.0	13
1 to 5 years	18.0	14
6 to 10 "	24.0	5
11 to 15 "	22.0	5
16 to 20 "	23.0	9
21 to 30 "	27.8	17
31 to 40 "	33.8	3

In the 89 cases of recessive status lymphaticus the thymus was weighable in 19 cases only. The average weights, grouped according to years, are shown in the following table:

⁵ Lancet, 1911, clxxxi, 752.

Age.	Average weight, grams.	Number of cases.
18 to 25 years	17.4	6
26 to 35 "	22.0	9
36 to 42 "	15.4	4

In the remaining 70 cases of recessive status lymphaticus the thymus was practically invisible to the naked eye and its position was occupied by a pad of fat or by fat and scattered glandular remnants, the whole corresponding, in a general way, to the normal outlines of the gland.

Sudden death in subjects of status lymphaticus has often been ascribed to pressure of the enlarged thymus upon the trachea. At Bellevue Hospital we have not been able to implicate the thymus as a mechanical factor in the production of death, the anatomical signs of tracheal compression and of death from suffocation never having been found, although sought. In this connection the figures above quoted are significant in that the heaviest thymus—namely, a gland of 70 grams—was greatly below the weight necessary for compressing the trachea, as shown by experiment, which, according to Tamassia,⁶ is at least 180 grams.

In the 118 cases of well-developed status lymphaticus the faucial tonsils were hyperplastic 61 times (51 per cent.), the lingual tonsils 58 times (49 per cent.) and the pharyngeal tonsils 45 times (37 per cent.). Peyer's patches and the solitary follicles were each hyperplastic in 105 cases (88 per cent.), sometimes in combination, at other times independently.

The spleen was described as small or normal in size in 68 cases (70 per cent.). In 26 cases the spleen was enlarged, but in all of them contributing factors were found to account for the enlargement, such as cirrhosis of the liver, sepsis, enteric fever, etc. This observation is of interest in connection with the statement of von Neusser that enlargement of the spleen is a factor in the diagnosis of status lymphaticus in the living patient. In our experience enlargement of the spleen is not a part of the pathology of status lymphaticus and should not be taken into clinical account except as it has to do with associated conditions.

The splenic lymphoid follicles were hyperplastic in 105 cases (88 per cent.).

The mesenteric lymph nodes were enlarged in 7 cases only, the axillary nodes 11 times, the inguinal nodes 12 times, the cervical nodes 15 times and the peribronchial nodes 5 times—in other words, changes in these situations are, for all practical purposes, negligible.

The figures referable to hyperplasia of the lymph nodes and intestinal follicles in recessive status lymphaticus form an interest-

⁶ Quoted by Blumer, *vide loc. cit.*

ing contrast to those quoted. Thus in 89 cases of recessive status lymphaticus the faucial tonsils were enlarged 25 times (28 per cent.), the lingual tonsils 32 times (36 per cent.), the pharyngeal tonsils 19 times (21 per cent.). Peyer's patches were enlarged 11 times (12 per cent.) and the solitary follicles 19 times (21 per cent.).

In the 89 cases of recessive status lymphaticus the spleen was described as normal or small in 52 (71 per cent.). The spleen was enlarged in 21 cases, in 17 of which enlargement was due to some accompanying lesion, such as chronic valvular disease, cirrhosis of the liver, etc.

The splenic follicles were hyperplastic in 37 cases (41 per cent.).

HISTOLOGY.—The histology of the thymus gland in most subjects of well-developed status lymphaticus presents nothing worthy of note other than hyperplasia of the cortical lymphoid follicles, but in many cases this is extreme. In other cases it is to be observed that there are large blood sinuses in the thymus and that they contain greatly increased numbers of lymphocytes. Whether this has any connection with the lymphocytosis which is sometimes encountered in the peripheral blood is a question to which, unfortunately, we are unable to give a definite reply. In Graves's disease, however, it is known that lymphocytosis is a frequent occurrence and that the thymus is hyperplastic often to an extraordinary degree. Shridde⁷ and others have pointed out that those patients in whom there is a lymphocytosis of 40 per cent. or over are dangerous operative risks and are liable to sudden death, which is in keeping with the known frequency of sudden death in Graves's disease in patients with persistent and hyperplastic thymi. That the lymphocytosis of Graves's disease is due to expulsion of thymic lymphoid cells into the circulation seems reasonably assured in view of the rich numbers of lymphocytes commonly to be found in the bloodvessels of the persistent and hyperplastic thymus. No doubt the hyperplastic lymph nodes also contribute their share of lymphocytes. In any event the number of lymphocytes in the circulating blood may be accepted as a more or less reliable index of the degree of lymphoid hyperplasia and should be taken into consideration in estimating operative risks in subjects of status lymphaticus.

Necrotic Changes in the Lymph Nodes. Microscopic examination of the lymph nodes in status lymphaticus shows the presence of vastly increased numbers of lymphocytes, the hyperplasia tending to bring about rearrangement of the architecture of the node by increase in the size and number of the so-called germinal follicles, and by overflow of cells into the tissue spaces and sometimes into the endothelial sinuses.

⁷ Deutsch. med. Wehnschr., 1911, xxiii, 1103.

In a considerable majority of all cases of well-developed status lymphaticus, but especially often in subjects who have met death suddenly and in response to apparently trivial provocation, the lymph nodes show a peculiar and characteristic change in the form of necrosis of the germinal areas attended by extensive disintegration of cells and the discharge of nuclear dust into the intercellular spaces. In still other cases of status lymphaticus, particularly in subjects who have passed the age of puberty, and in recessive status lymphaticus, the germinal follicles often show almost complete replacement by whorl-like collections of spindle cells representing, apparently, connective-tissue elements. Lying among the spindle cells are to be made out rather large polyhedral forms resembling degenerate cells of the type of large lymphocytes. The cytoplasm of both the spindle and polyhedral cells stains pink with eosin, so that the follicle stands out in contrast to the deep blue of the small lymphocytes in the immediate vicinity. The changes in question were originally described by Lartigau,⁸ later by Blumer,⁹ and, in this laboratory, we do not hesitate to make the microscopic diagnosis of status lymphaticus from these findings alone. We have yet to observe them in any condition other than status lymphaticus. They occur not only in follicles of the lymph nodes themselves but in those of the intestine, the lingual, faucial and pharyngeal tonsils, in the follicles of the spleen and, on at least one occasion, I have seen them in the hyperplastic follicles in the interstitial tissues of the thyroid gland from a case of Graves's disease.

The histological changes in the several lymphoid depots in the older cases of status lymphaticus, including, of course, the recessive type, reveal simple diminution in the numbers of lymphoid cells usually with but sometimes without the presence of necrotic, degenerative or fibrotic alterations in the germinal follicles.

The histology and distribution of the lymphoid tissues are, I believe, of fundamental importance in the interpretation of anaphylaxis as a cause of sudden death and of certain convulsive phenomena occurring in subjects of status lymphaticus.¹⁰ Thus, the lymphoid tissues are most abundantly developed in youth and early adolescence, tending to disappear as age advances, which is in keeping with the observation that in status lymphaticus the danger of sudden death is greatest during that period of life in which the lymphoid tissues are most flourishing and is almost unknown in the recessive stage. It is likewise significant that in status lymphaticus those lymphoid tissues which display the highest degree of hyperplasia are to be found in the mucous membrane of the gastro-intestinal tract, where, of all the lymphoid structures, they are the ones most actively

⁸ Ann. Surg., 1902, xxxv, 745.

⁹ Johns Hopkins Hosp Bull., 1903, xiv, 270.

¹⁰ Symmers: Am. Jour. Dis. Children, 1917, xiv, 463.

engaged in the process of filtration, in the course of which they are constantly subjected to the destructive action of a great variety of toxic substances, both chemical and bacterial. In children suddenly dead with all the physical attributes of status lymphaticus, microscopic examination of the lymphoid tissues throughout the body shows, with rare exceptions, myriads of necroses in the germinal follicles of the sort already described. These changes indicate, I believe, that sudden death in status lymphaticus is connected with the release of nucleoproteids formed as a result of destruction of innumerable germinal follicles. It is scarcely conceivable, however, that death is directly traceable to the toxemia produced by sudden and simultaneous destruction of a large number of follicles, as maintained by Blumer,¹¹ since the interval between injury and death is far too short, in the majority of cases, to permit so many necrotic lesions to occur throughout such a wide distribution. It is more probable, I think, that death is of the nature of an anaphylactic reaction, sensitization being expressed in structural terms by the necrotic germinal follicles, and, chemically, by the release of nucleoproteids which, although not strictly foreign, are none the less pathological, and are comparable, in a toxicological sense, to alien products. Previous to the expiration of the so-called anaphylactic incubation period the lymph nodes are again subjected to the action of destructive substances which serve to bring about still further disintegration of germinal nuclei, thus providing the requisite quantity of specific proteid to complete the anaphylactic cycle. The destructive substances in question may be introduced in the form of antitoxins hypodermically injected, or as vaccines applied by scarification or otherwise, or as substances which have escaped destruction or modification by the hyperplastic lymphoid follicles in the intestinal tract, or which have been manufactured in the process of shock induced even by such simple procedures as the prick of a needle, sudden immersion in cold water and similar events.

That acute necroses may occur in irregular showers is shown by the presence of all stages of both the necrotic and reparative processes in the same lymph node or in different nodes in the same body. This fact is of moment in that the anaphylactic reactivity of the body is determined by the number of acute necrotic lesions in the germinal follicles, or, in other words, the anaphylactic incubation period in man, as in experimental animals, varies with the initial dose of the sensitizing proteid. For example, in guinea-pigs injected with small amounts of horse serum from twelve to fourteen days suffice for sensitization. With larger doses, however, the interval may be extended to weeks or months. In subjects of status lymphaticus it is naturally to be expected that early sensiti-

¹¹ Vide loc. cit.

zation follows a small shower of necroses and that larger showers are succeeded by a longer period of incubation, the reactive ranges thus varying within wide limits, both in the matter of time and intensity. At one moment the tissues are exquisitely tuned and await only the receipt of a sufficient quantity of specific protein to react violently, even to the extent of sudden death, while at another moment events are so timed that the same quantity of specific protein exerts no such effect, a fact which tends to explain why certain subjects of status lymphaticus survive surgical and other procedures which, in others, are attended by disaster. In this instance it is apparently a question of anaphylactic reactivity dependent upon the number of acute necrotic lesions in the lymph nodes and upon the interval which has elapsed since their inception.

Idiopathic Epilepsy. The theory of anaphylactic shock is also applicable, I believe, to the convulsive disorders of certain subjects of idiopathic epilepsy, most of whom, according to Karpas, present the typical configuration of status lymphaticus. It impresses me as a matter of extreme significance that the victims of idiopathic epilepsy may cease to have convulsive seizures at an age when involution of the thymus gland is to be expected or has actually taken place. In the case of a negro, aged twenty-six years, who recently came to autopsy at Bellevue Hospital, there was a history of epileptic seizures attended by biting of the tongue that occurred with frequency throughout early life, but which diminished at about the twelfth year and disappeared by the fourteenth. Death was due to dilatation of the heart, and autopsy revealed the characteristic configuration of status lymphaticus, partial atrophy and fatty replacement of the thymus gland, and irregularly distributed atrophic changes in the lymphoid tissues elsewhere.

If it is true that idiopathic epilepsy and status lymphaticus stand in relationship to one another the suggestion appears to be not out of place that subjects of idiopathic epilepsy might readily derive benefit from exposure of the thymus and spleen, possibly the intestines, to the x -rays, since it is known that radiation discourages proliferation of lymphoid tissues and brings about atrophy of those already present.

(b) THE CARDIOVASCULAR SYSTEM: Of the 249 cases of status lymphaticus and recessive status lymphaticus encountered among the first 4000 autopsies at Bellevue Hospital the heart was described as small or normal in size in 127 (51 per cent.). In 46 cases the heart was enlarged, due, in every instance, to inherent valvular disease or to chronic interstitial nephritis, emphysema and similar causes.

Of the 249 cases the aorta was described as hypoplastic in 101 cases (40.5 per cent.). In 71 of these cases hypoplasia was determined by actual measurement of the relative width of the pulmo-

nary artery and the aorta. In 8 cases the measurements were the same. In the remaining 63 cases the average width of the pulmonary artery and aorta was 6.6 cm. and 5.7 cm. as opposed to the normal measurements of 6.5 to 7 cm. and 7 to 7.5 cm. In 78 cases (31 per cent.) the elasticity of the aorta was increased and in 66 cases (26.5 per cent) the vessel was described as unusually thin.

Status Lymphaticus and Aortitis: It is worthy of remark that in 249 cases of status lymphaticus there were 37 instances (about 15 per cent.) in which anatomical changes due to syphilis were detected in various parts a slightly higher percentage than that usually accredited to subjects coming to autopsy in Bellevue Hospital, 6.5 per cent. in a series of 314 cases¹² of late acquired syphilis, having shown syphilitic lesions. Of the 37 cases of syphilis associated with status lymphaticus the aorta was the seat of syphilitic lesions in 15 instances (40 per cent.). In 4 cases the aorta from commencement to bifurcation was the seat of syphilitic aortitis, in 9 cases the changes were advanced but were limited to the arch, in 1 case there was syphilitic aortitis of the arch and thoracic aorta and in 1 case a small aneurysm of the sinus of Valsalva was imposed upon a limited syphilitic aortitis of the ascending aorta. In one of these cases syphilitic aortitis was associated with extensive chronic interstitial myocarditis and in another multiple gummata were present in the heart muscle. It appears therefore that syphilitic aortitis which, in the ordinary course of events, is present in somewhat over 55 per cent. of all syphilitic subjects investigated postmortem at Bellevue Hospital is neither more nor less frequent or severe in status lymphaticus than otherwise and that the thinness and increased elasticity of the aorta in status lymphaticus is not of great moment so far as increased susceptibility to syphilitic aortitis and aneurysmal dilatation are concerned. Moreover, it is probable that the increased elasticity of the vessel is a detriment to those mechanical factors which favor aneurysmal dilatation.

Acute Gelatinous Aortitis: In the 249 cases of status lymphaticus there were 15 cases of the acute gelatinous aortitis described by the French. This lesion is characterized by swelling, opacity and stickiness of the intima, attended, microscopically, by enlargement and vacuolation of the endothelial cells. In our cases it was associated with croupous pneumonia 8 times, bronchopneumonia 4 times, suppurative pericarditis, sepsis and acute miliary tuberculosis once each. The lesion, so far as I am aware, has no practical significance.

Status Lymphaticus and Cerebral Hemorrhage in the Young: In status lymphaticus the cerebral vessels, particularly the arteries entering into the formation of the circle of Willis and the branches

¹² Symmers: Jour. Am. Med. Assn., 1916, lxvi, 1457.

which emerge therefrom, are often small in caliber and extremely thin and delicate.¹³ As seen at autopsy the larger vessels at the base, for example, are collapsed, one wall lying against the other and, when removed from the body and viewed by transmitted light, they are easily translucent. Upon microscopic examination these vessels show simple hypoplastic alterations, the deficiency being most marked in the muscular coat, which is distinctly less developed than in normal circumstances. The exact incidence of these changes in status lymphaticus has not been determined but the association has been noted with such frequency as to leave no doubt that the two are companion manifestations of one and the same underlying developmental defect.

Hypoplasia of the cerebral vessels in subjects of status lymphaticus is of profound importance from the stand-point of sudden death, not only sudden death ensuing spontaneously, but in subjects who have been exposed to a degree of injury which, in normal individuals, would be regarded as insignificant. In the latter group of cases its medicolegal application cannot be overestimated. In the experience of Dr. Otto H. Schultze, the pathologist to the district attorney's office in the city of New York and in our own postmortem work at Bellevue Hospital, cerebral hemorrhage in young, non-syphilitic subjects of status lymphaticus occurs a number of times in the course of every year, and is due to rupture of hypoplastic cerebral arteries occurring spontaneously or upon the receipt of apparently trivial traumatism or under the influence of physical strain or intense excitement. In such subjects, therefore, any influence which causes sudden increase in intracranial blood-pressure may be disastrous, such as heavy lifting, straining at stool, the tension of argument, fighting, etc.

In the 249 cases of status lymphaticus, sudden death due to spontaneous rupture of a hypoplastic cerebral artery occurred 7 times (3 times in men and 4 times in women), all of them under thirty years of age, none of them presenting syphilitic or precocious arteriosclerotic changes in the vessels of the brain or elsewhere. The clinical symptoms were those of cerebral hemorrhage and death occurred rapidly. In one of these cases the patient, a clerk, aged twenty-eight years, walked into the hospital complaining of headache of two or three days' duration, weakness and nausea. Death occurred a few hours after admission. In a second case the patient, an elocutionist, was apparently perfectly well until the morning of admission, when she suddenly became unconscious and died with signs of complete left-sided hemiplegia. In a third case the patient, a factory girl, aged nineteen years, upon arriving home one night suddenly fell in the doorway, shrieked loudly, and the

¹³ Wiesner: Verh. d. deutsch. path. Gesellsch., 13 Tagung, 1909.

ambulance surgeon who went to her relief found complete paralysis of the left side of the body. Death occurred the following day. In these as in the remaining 4 cases autopsy revealed rupture of hypoplastic cerebral bloodvessels, hemorrhage occurring in the pons and medulla, the ventricles, the lenticular and caudate nucleus, the lenticular nucleus, the cerebellum, the temporal and right occipital lobe respectively. In still other instances, however, hemorrhage is confined to the pia arachnoid.

In the past year Dr. Schultze tells me that in one of his cases a boy fell dead while engaged in a fisticuff, and another, a young woman, died while straining at stool. It is quite apparent, therefore, that the problem abounds in medicolegal possibilities and that the clinical or postmortem recognition of status lymphaticus and its not infrequent association with this form of sudden death is of paramount importance, since failure properly to appreciate the connection between the two may jeopardize a man's life or liberty.

Cerebral hemorrhage in the young is oftenest ascribed to rupture of miliary aneurysms, which are usually regarded as of syphilitic origin. In many cases their syphilitic nature is apparent. In other instances, however, they appear to arise purely on the basis of congenitally hypoplastic bloodvessels. In the syphilitic cases aneurysmal dilatation occurs at a point in the muscular coat or elsewhere marked by the presence of minute gummata, with or without central necrosis, thus providing a field of diminished resistance. In 5000 autopsies at Bellevue Hospital miliary aneurysms of syphilitic origin occurred 7 times. On the other hand, there were 9 cases in which miliary aneurysms occurred in congenitally hypoplastic bloodvessels without the intervention of degenerative or inflammatory changes traceable to syphilis. Four occurred in females, the youngest subject a girl, aged seventeen years, and 5 in males, the oldest subject a man aged sixty-four years. The average age was forty-two years. In all of these cases the vessels at the base of the brain were described as extremely delicate, the walls being translucent and collapsed. In 5 cases the hypoplastic cerebral vessels were encountered in individuals presenting the anatomical changes in the kidney incident to chronic interstitial nephritis. In 2 of these cases there were small sclerotic foci to be made out in the cerebral arteries concerned, thus affording a favorable site for aneurysmal dilatation. In the other 4 cases the hypoplastic vessels were found in subjects of status lymphaticus. One of these exhibited the anatomical signs of chronic interstitial nephritis. The other 3 presented acute vegetative lesions in the heart valves, which, possibly, contributed to aneurysmal dilatation of the cerebral vessels by the discharge of infective emboli and the production of inflammatory lesions at the point of lodgment.

Status Lymphaticus and Caisson Disease: Hypoplasia of the smaller bloodvessels in status lymphaticus is apparently an element

of danger in workers in compressed air, 5 cases of caisson disease having been examined postmortem in Bellevue Hospital in individuals showing the characteristic stigmata. All of them were young, muscular adults. Three presented the configuration of status lymphaticus. In 2 of them the protocols were silent on this score. In all of them the aorta was markedly hypoplastic. In 2 the thymus was described as enlarged, in the other 3 the thymus weighed 27, 35 and 25 grams respectively. In 4 cases the splenic follicles were enlarged. In 1 case the lingual and faucial tonsils and the solitary and agminated follicles in the intestine and the mesenteric nodes were unduly prominent and in 3 cases the intestinal follicles alone were hyperplastic. All of the bodies presented innumerable odorless air bubbles in the vessels of the brain and trunk. From these 5 cases, which represent the sum total of our experience in caisson disease during a period when active tunnelling operations were under way in New York City, it is quite apparent that status lymphaticus constitutes a contra-indication to the acceptance of a workman for duty in an atmosphere of compressed air even though decompression be brought about with scientific exactitude. Just why this should be true is not apparent, but it probably has something to do with defective permeability of congenitally hypoplastic bloodvessels, so that tissues saturated with nitrogen under pressure yield this gas under decompression in such quantities that the blood cannot take it into solution and it circulates as emboli.

Status Lymphaticus and Emotional Instability: Emerson,¹⁴ working in the alcoholic wards at Bellevue Hospital, examined 1000 patients suffering from the effects of attempted suicide and from cocaine, morphin, heroin, alcohol and similar habituating drugs. Of this number 220 (22 per cent.) showed most or all of the physical stigmata of status lymphaticus. I have had occasion to note the characteristic configuration of status lymphaticus in sufferers from neurasthenia and in certain primitive races. In the autopsy rooms at Bellevue Hospital, which are utilized by the several coroners' physicians and by Dr. Schultze, of the district attorney's office, for the performance of autopsies in medicolegal cases, it is a matter of almost daily observation that suicides and degenerates, and gunmen and other criminals who have met death by violence, present the characteristic conformation and anatomical changes of status lymphaticus. According to the combined statistics of Bartels¹⁵ and Miloslavich,¹⁶ amounting to 232 cases of suicide, 80.5 per cent showed the signs of status lymphaticus at autopsy. Among epileptics and the insane the condition is common (Karpas).

It is scarcely conceivable that status lymphaticus occurring with such frequency among such a diversity of individuals of unstable

¹⁴ Arch. Int. Med., 1914, xiii, 169; Med. Press, October 15, 1913, p. 418.

¹⁵ Wien. klin. Wehnschr., 1908, lv, 1826.

¹⁶ Virchows Arch., 1912, cviii, 44.

emotional qualities could be purely accidental. It seems more within reason to assume that congenitally hypoplastic bloodvessels are under indifferent vasomotor control and that this is not without influence upon mental poise.

Status Lymphaticus and Exophthalmic Goitre: The association of status lymphaticus and exophthalmic goitre, while not constant, is common, and is particularly noteworthy in connection with the incidence of status lymphaticus among the emotionally unstable. In 6 cases of exophthalmic goitre investigated postmortem at Bellevue Hospital, signs of status lymphaticus were present in 5, in some better developed than in others. In 3 cases the thymus was enlarged, weighing 45, 64 and 26 grams respectively, and in all the configuration was typical and the lymphoid tissues were hyperplastic. In a fourth case the thymus was partially replaced by fat, but glandular remnants were still visible and the follicles in the spleen were numerous and large. In a fifth case the configuration was typical, but the lymphoid tissues had undergone marked regression. It is furthermore interesting to record that, with other pathologists, I have not uncommonly seen hyperplastic follicles in the stroma of the thyroid gland removed from subjects of exophthalmic goitre at operation or autopsy. Capelle¹⁷ collected 60 cases of Graves's disease from the literature. In 44 per cent. the patients died from intercurrent affections, and in all of them the thymus was persistent and hyperplastic. Of those dying of Graves's disease without associated lesions, 82 per cent. presented enlargement of the thymus, while in cases of sudden death following operation for removal of the thyroid the thymus was hyperplastic in all.

It has long been known that derangement of the emotional nervous system, manifested by intense grief or fear, may rapidly be followed by the symptoms of exophthalmic goitre, that exophthalmic goitre frequently is implanted in young women of uncertain emotional balance, sometimes in a family whose genealogy is marred by a history of epilepsy, insanity and kindred disorders, and that a certain proportion of all cases of Graves's disease follows influenza or streptococcal throat infection, either of which is prone to leave its victim mentally perturbed. That Graves's disease not infrequently follows shock has been amply exemplified by the present war, numbers of soldiers exposed to the terrifying vicissitudes of trench life having been invalided with symptoms of Graves's disease varying in intensity from simple tachycardia and muscular tremors to the fully developed picture.¹⁸ It seems not improbable that exophthalmic goitre, in certain subjects of status lymphaticus at least, is the result of disturbances in an already unstable nervous system that have so altered the function of the thyroid gland as

¹⁷ München. med. Wehnschr., 1908, lv, 1826.

¹⁸ Stoney: Lancet, April 8, 1916, p. 777; *ibid.*, White and Hernaman-Johnson, January 8, 1916, p. 78.

permanently to externalize the physical attributes of fear as expressed by protruding eyeballs, irregularity and increased rapidity of the heart's action, muscular tremors, clammy sweats, pallor and the like. In other words, the subject of status lymphaticus, as a result of hereditary anatomical imperfections, appears to be more susceptible to those influences, infective, psychic or otherwise, which precipitate exophthalmic goitre than the individual who more nearly approaches the normal. This hypothesis, at all events, is more in consonance with established facts than the extreme view of certain students of the French school who maintain that Graves's disease is the direct result of disturbances in the thymus gland rather than the thyroid, and who have advocated and actually practised thymectomy for its relief. The alternative, as far as I can judge, is to dismiss the association of status lymphaticus and Graves's disease as accidental, and this seems scarcely justified by circumstances.

Chlorosis: It has been pointed out by Virchow that in chlorotic girls the aorta is hypoplastic and the genitalia, notably the uterus, of the infantile type. Not only are these deficiencies common to status lymphaticus in the female, but it is a matter of observation that chlorotic girls almost invariably present a skin of exquisite texture and that the normally graceful outlines of the body are accentuated and the subcutaneous fat well preserved. That the vasomotor system is easily disturbed is shown by frequent changes in color, by the paradoxical association of rosy cheeks with pronounced anemia—the so-called chlorosis rubra—by dermatographia and by a tendency to syncope which is often out of proportion to the severity of anemia, while emotional disturbances are notoriously common. In short, the anatomical signs and the symptoms of chlorosis suggest that this form of anemia is an incidental and fugitive condition in girls with status lymphaticus.

Status Lymphaticus and Acute Infection: There is very little in the literature bearing on the susceptibility of subjects of status lymphaticus to infection. Daut¹⁹ has shown, however, that over 25 per cent. of patients dying of diphtheria present the anatomical changes of status lymphaticus. Elser's²⁰ observations on epidemic cerebrospinal meningitis lead him to the conclusion that status lymphaticus, occurring in over a quarter of all subjects examined at autopsy, constitutes a predisposing factor in this variety of infection, and, in addition, he noted that the issue is apt to be rapidly fatal in patients of this sort. Blumer²¹ has reported a case of tetanus in a boy, aged twelve years, in whom death occurred after an unusually short illness.

In 249 cases of status lymphaticus investigated postmortem at

¹⁹ Jahrbuch. f. Kinderheilk., 1898, xlvii, 141.

²⁰ Jour. Med. Research, 1905, ix, 89.

²¹ Vide loc. cit.

Bellevue Hospital acute infective lesions occurred in 222, or in 88 per cent., distributed thus:

Acute infective endocarditis	51
Croupous pneumonia	36
Epidemic cerebrospinal meningitis	33
Bronchopneumonia	21
Sepsis	15
Acute general miliary tuberculosis	14
Suppurative otitis media	10
Acute miliary tuberculosis of lungs	6
Tuberculous pneumonia	5
Pyonephrosis	5
Enteric fever	5
Pneumococcal meningitis	3
Diphtheria	3
Abscess of lung	3
General peritonitis	3
Empyema	2
Purulent cystitis	1
Purulent tonsillitis	1
Ulcerative colitis	1
Erysipelas	1
Smallpox	1
Abscess of the mouth	1
Abscess of the spleen	1

Status Lymphaticus and Acute Infective Endocarditis. Of the 249 cases of status lymphaticus the heart valves were involved 88 times, but in 37 of these the valvular lesions were chronic and have been excluded from the above list. Of the 37 chronic valvular lesions the youngest occurred in a subject of eight years and the oldest in a man of sixty-two years. The average age was 39.9 years. The aortic valves were alone involved in 9 cases—3 were stenotic lesions and 3 occurred in syphilitic subjects. The mitral valves alone were involved in 12 cases, 5 of them being stenotic lesions. The aortic and mitral valves together were concerned in 10 cases and the aortic mitral and tricuspid together were involved 4 times, the tricuspid valves alone in 2 cases.

Acute infective lesions of the heart valves were superimposed upon chronic sclerotic valvulitis in 26 cases. The youngest subject was a fourteen-year-old boy and the oldest a man, aged forty-five years. The average age was 22.5 years. The aortic valves were alone involved in 5 cases, the mitral valves in 4, the mitral and aortic valves together in 9, the aortic, mitral and tricuspid together in 4, the mitral and tricuspid in 3 and all the valves of the heart in 1.

Acute infective lesions occurring in otherwise apparently healthy valves were encountered 25 times. The youngest subject was aged four and the oldest forty-four years. The average age was 24.4 years. The aortic valves were alone concerned 6 times, the mitral valves 4 times, the aortic and mitral valves 8 times, the aortic, mitral and tricuspid 3 times, the mitral and pulmonary, the mitral, pulmonary and tricuspid, the aortic and tricuspid and the mitral and tricuspid once each. Associated with the lesions enumerated the left

auricle was the seat of vegetative endocarditis twice, the wall of the left ventricle 4 times, and there were vegetations in the arch of the aorta in 3 cases and in the pulmonary artery once.

In 249 cases of status lymphaticus, therefore, there were 88 cases of endocarditis (35.3 per cent.), of which number 51, or 57.8 per cent., were acute. It seems scarcely possible to evade the conclusion that status lymphaticus is a distinct predisposing factor in those infective processes which exert a selective action on the heart valves and in which, in many cases, the provocative micro-organism enters the body through the tonsils. Even though the 26 instances of acute infective endocarditis superimposed upon valves already the seat of sclerotic lesions be excluded on the ground that local conditions were propitious for infection, the fact still remains that about 10 per cent. of all subjects of status lymphaticus present acute infective lesions of the heart valves—a point quite worthy of remembrance in dealing with obscure symptoms of infection in patients of this type.

Status Lymphaticus and Epidemic Cerebrospinal Meningitis: In 1906-07 there was an epidemic of cerebrospinal meningitis in New York City and 55 cases were submitted to autopsy at Bellevue Hospital. Of this number 33 (60 per cent.) occurred in young subjects of status lymphaticus. The meningococcus was isolated in every instance. The thymus was described as greatly enlarged in 4 cases, very large in 2 cases, large in 6 cases, persistent in 1 case, and in 7 cases the weights were recorded as 15, 12, 68, 20, 27, 28 and 31 grams respectively. Of the 33 cases it was possible to ascertain the duration of symptoms in 30, and death occurred as shown in the following table:

Number of cases.	Duration of symptoms.
1	1 day
8	2 days
4	3 "
4	4 "
4	5 "
2	8 "
1	11 "
1	13 "
1	17 "
1	20 "
1	21 "
1	(healed) 45 "
1	" 59 "

In 23 of the 30 cases (70 per cent.) death occurred after the lapse of an average interval of 3.4 days, which, of course, is an exceedingly short period of illness. In other words the subject of status lymphaticus is extremely susceptible to infection by the meningococcus and the disease is apt to pursue a remarkably rapid course. Here, again, the hyperplastic lymphoid tissues in the tonsils and nasopharynx are probably remiss in their function as part of the body's filtration plant.

Status Lymphaticus and Enteric Fever: In 6562 autopsies at Bellevue Hospital there were 81 cases of enteric fever, only 5 of which are included in the list of general infections above. Of the total number, 16 (19.7 per cent.) occurred in subjects of status lymphaticus, 12 times in males and 4 times in females. The youngest subject was a boy, aged seventeen years, the oldest a man, aged forty years. The average age was 25.5 years. All of them, with 3 exceptions, were subjects of well-developed status lymphaticus, the remaining 3 cases being of the recessive type. In all of the cases the typhoid bacillus was isolated in pure culture.

Of the 16 cases it was possible to ascertain the duration of illness in 13, dating from the time that the several patients actually took to bed. The duration was as shown in the following table:

Number of cases.	Duration of illness.
1	3 days
1	4 "
1	5 "
1	10 "
2	11 "
1	14 "
1	16 "
1	17 "
1	18 "
2	24 "
1	26 "

The average duration of illness was therefore fourteen days, which for enteric fever is far short of the average expectation in fatal cases.

In the 16 subjects of status lymphaticus dead of enteric fever the reaction of the lymphoid tissues in the intestine varied noticeably. In one type of case the ulcers in the intestine were numerous, large and deep and the non-ulcerated follicles in the vicinity were only moderately hyperplastic. Seven such cases occurred, and of this number 3 were attended by perforation and purulent peritonitis, 2 by ulcers which extended into the musculature and 1 by ulcers which were limited externally by the serosa. In a second type of case the solitary and agminated follicles were greatly increased in size and the ulcerations were superficial, sometimes to such an extent that it was difficult to make them out by the unaided eye. Changes of this type were noted in individuals who had not yet passed the second week, death apparently being due to intense toxemia. In the Bellevue series 7 such cases occurred. In 5 of these cases the solitary follicles and Peyer's patches were markedly hyperplastic and superficially ulcerated. In another case the ileocecal orifice was almost closed by an enormously hyperplastic, congested and superficially ulcerated Peyer's patch, the patches in the ileum just above being enlarged to such an extent that they projected into the lumen as mushroom-like growths, the solitary follicles standing out as tab-like bodies. In another case

the ileocecal Peyer's patch appeared as a polypoid outgrowth and was richly congested and superficially ulcerated. In a third type of case the ulcerated areas displayed signs of healing. Two examples were encountered. In 1 case the ileum showed numerous small ulcers, many of which were surrounded by a whitish zone. In the colon, however, were many large ulcers and an enormous collection of free blood, and no doubt the lesions in the large intestine represented an expression of reinfection. In a second case of this type the small and large intestine showed numerous smooth, plaque like areas of ulceration.

(c) **THE GENITALIA.** In male subjects of status lymphaticus, according to our observations at Bellevue Hospital, the penis is small in about 12 per cent. of all cases, while the glans is pointed or acorn-shaped and small in about 18 per cent. In a considerable number of all cases microscopic examination of the testicles showed the peculiar connective-tissue hyperplasia described by Kyrle²² as a developmental defect in the testicles of many young subjects. The function of spermatogenesis was apparently active.

In female subjects of status lymphaticus the uterus is hypoplastic in a considerable number of cases.

In view of the fact that the cortex of the suprarenal capsule is embryologically related to the testicle in the male and the ovary in the female it is worthy of note that Norris and Wiesel have pointed out the almost constant occurrence of hypoplasia of the suprarenal cortex in subjects of status lymphaticus.

(d) Finally, it is to be mentioned that subjects of status lymphaticus not uncommonly show such peculiarities as supernumerary lobulations in the lungs and similar unimportant although interesting developmental anomalies.

A STUDY OF OCHRONOSIS.

BY N. W. JANNEY, M.D., PH.D., CAPT., M. R. C.,
NEW YORK.

(From the Montefiore Hospital, New York City.)

AN excellent opportunity to observe this rare and obscure disease was recently afforded by a case coming to autopsy. This case was of unusual interest, as it presented a strong clinical resemblance to alcaptonuria. Investigation of the melanotic pigment present led, however, to the diagnosis of ochronosis with melanuria, no direct relation to the alcaptonuric condition being discovered.

In the present article the writer's investigation of the metabolism

²² Wien. klin. Wehnschr., 1910, No. 45, p. 1583.

of ochronosis is reported.¹ In the first part of the paper are reported the results of the chemical studies, which are applied in the succeeding pages in a discussion of the pathogenesis of ochronosis and the relation of ochronosis to alcaptonuria.

CASE ABSTRACT.—M. K., aged forty years, male. Chief complaints, weakness, stiffness of joints and black discoloration of the urine. Duration of the disease, eighteen months. Examination showed emaciation, bluish pigmentation of the scleræ, aural cartilages and axillæ; arthritis of spine and various larger joints. The patient's cachexia increased after admission, decreasingly smaller amounts of the melanotic urine being passed until death ensued three weeks after admission. Autopsy disclosed intense black pigmentation of the superficial bones, especially the ribs, also the presence of melanotic calculi in the prostate. Histological examination showed the typical pathological changes originally described by Virchow under the name of *ochronosis*, which refers to the yellow color of the pigment granules under the microscope. A prostatic calculus and a rib cartilage were reserved for chemical examination.

Prostatic Calculus. The calculus was rounded in form, about 1 cm. in diameter; after drying in the air it measured about one-half this size. It was brown black in color and consisted of several lobes. It was amorphous throughout. A cavity in the center may have represented the site of a corpus amalaceum. An outer brown-black layer was carefully removed, exposing the coal-black pigment which made up the bulk of the calculus. The latter was used for combustion. Weight of the air-dried concretum was 0.12 gm.

Elementary analysis by courtesy of Dr. P. A. Levene, Rockefeller Institute, New York City: 0.0832 gm. dried in vacuum at 100° gave 0.1572 gm. CO₂ and 0.0392 gm. H₂O. Carbon = 51.52 per cent. Hydrogen = 5.27 per cent. There remained after combustion 0.0062 gm. ash = 7.45 per cent.

Urinary Examination. The patient passed small amounts of amber-colored urine, which became dusky brown on standing exposed to the air. Quantity 300 to 500 c.c. per twenty-four hours. Routine examination: Specific gravity, 1010. Albumin, acetone, diacetic acid, bile, blood and indican negative. Microscopically, crystalline and amorphous urates, occasionally hyaline casts. The fresh urine containing the chromogen was amber-colored. It gave a dark brown coloration on being boiled with Benedict's solution, a slight amount of green precipitate, settling out on standing. Reduced ammoniacal silver solution and alkaline picric acid solution. Unaffected by bromine water immediately, but on standing

¹ A preliminary report of this work was presented with Dr. B. S. Oppenheimer before the section of Internal Medicine, New York Academy of Medicine, March, 1916. In connection with the present study, further investigations of ochronosis were made by my former co-workers, Drs. B. S. Oppenheimer and B. S. Kline. On account of their absence on military duty the report of their work will be deferred until a later date.

a reddish coloration developed. With ferric chloride a green color was produced which vanished immediately. With lead acetate there was the usual white precipitate. With barium hydroxide a brown precipitate (melanin), the supernatant fluid becoming colorless. Boiled with strong nitric acid a yellow color is produced. Treated with potassium bichromate and sulphuric acid or with sodium hydroxide and potassium permanganate a dark brown to black color, evidently due to melanin, appears even in the cold. Black pigment formation readily took place on passing an air current through the urine made alkaline with sodium carbonate or sodium hydroxide.

All the subsequent tests and examinations were made on the urine after pigment formation had taken place. The urine, dusky yellow to black in color, reduced Benedict's solution immediately with heavy precipitate. Reduces picric acid solution, ammoniacal silver solution but not bismuth oxynitrate. Barium precipitates the bulk of the pigment. Lead acetate precipitates practically all the pigment, together with the urochromes, leaving a clear supernatant liquid. The urine does not form gas on fermenting with yeast. No rotation on polariscopic examination.

The presence of glucose could be excluded by the negative result of the fermentation test, optical inactivity of the urine and failure to reduce bismuth oxynitrate solution.

Attempts to Isolate Homogentisic Acid. In view of the tendency of homogentisic acid to decompose, the urine for this examination was collected in bottles containing a little dilute hydrochloric acid and preserved in an ice-box.

1. *According to Ester Method of Schumm.*² The total urine voided during three days, including portions containing the amber-colored chromogen as well as the melanin, was acidulated, and evaporated on the water-bath down to a volume of 300 c.c. which was extracted in Lind's rotary extraction apparatus for a period of five hours with ether. On evaporation of the ether about 3 c.c. of syrupy residue was obtained. The ether-soluble acids were evidently not increased in amount. The ethereal residue was dissolved in 200 c.c. alcohol, boiled one hour under a reflux condenser after the addition of 40 c.c. strong hydrochloric acid. The cooled liquid was diluted to about 60 c.c. with water, made weakly alkaline with sodium hydroxide and repeatedly extracted with ether. On evaporation of the combined ethereal extracts only a minute quantity of brown amorphous pigment matter remained. Neither homogentisic nor other esters, nor, indeed, crystalline substances of any kind, was found.

2. *According to the writer's procedure*, 3 liters of mixed urine were acidulated and evaporated to small bulk and extracted five hours

² München. med. Wehnschr., 1904, 1599.

in the special apparatus as previously. The small syrupy residue obtained on evaporating the ethereal extract was diluted with 100 parts of water and lead acetate added in excess. Aside from a small yellowish precipitate of resinous texture, which formed immediately, no other deposit appeared even on standing. The yellow precipitate was filtered off, dried, suspended in ether and decomposed by hydrogen sulphide. After removal of excess of hydrogen sulphide by an air current and the lead sulphide by filtration the residue left on evaporation of the ether weighed 0.1 gm. It crystallized out of water in small crystals which failed to lose water, also to sublime, and which melted at a temperature other than does homogentisic acid. *Homogentisic acid was therefore not present in the urine of this case.*

Method Employed for Preparation of the Melanin from Urine. This procedure depends on the writer's observation that maximum quantities of the pigment are precipitated from the melanotic urine by the addition of a like volume of 25 per cent. acetic acid to the neutral urine. Four hundred cubic centimeters of urine containing the chromogen was made distinctly alkaline by adding a little sodium carbonate solution and an air current passed through it for twenty-four hours. The pigment was fully developed from the chromogen at the end of this time. To the black urine an equal volume of 25 per cent. acetic acid was added and the mixture allowed to stand overnight. Owing to difficult filtration the supernatant fluid was removed from the precipitated pigment by means of a siphon and the pigment thoroughly washed by decantation with 12.5 per cent. acetic acid, employing twenty or more changes of the wash fluid. The melanin was next dissolved in a small amount of concentrated sodium carbonate solution and strong acetic acid added to neutralization. The pigment was then reprecipitated by the addition of a like volume of 25 per cent. acetic acid, collected on a filter, washed thoroughly with 12.5 per cent. acetic acid, twice with water, then dried in a desiccator, thoroughly extracted with alcohol, followed by ether and dried in vacuum. From 400 c.c. urine 0.55 gm. purified pigment could thus be obtained. The supernatant liquid obtained from the precipitation of pigment from the urine was evaporated to small bulk at a low temperature and the like volume of 25 per cent. acetic acid added. Additional melanin, 0.1 gm., was obtained in this way.

Additional pigment was obtained by boiling a costal cartilage with strong hydrochloric acid until solution took place, neutralizing, precipitating with an equal volume of 25 per cent. acetic acid and reprecipitating from 10 per cent. sodium carbonate solution, as in the case of the urinary pigment. 5.27 gm. air-dried rib yielded 0.120 gm. purified pigment. The rib pigment had the same characteristics as the urinary pigment.

The axillæ of the ochronosis patient were stained bluish black

with pigment particles which showed the same color reactions of the urinary pigment.

The pigment of the present case exhibited in general similar characteristics to melanins previously obtained from the urine and tumors of cases of melanosarcoma. Such pigments have been exhaustively studied by Mörner.³ Accordingly the reactions found by this investigator to be characteristic for these tumor pigments were carried out on our preparations. The results of this comparative study are now mentioned. Barium hydroxide precipitated most of the pigment out of the urine. The precipitated melanin dissolved in various alkalis, sodium hydroxide, sodium carbonate, ammonium hydroxide, giving a black solution. From the sodium hydroxide solution the pigment could be precipitated by acetic acid added in excess. To the filtrate from the barium hydroxide precipitate, lead acetate was added. All the pigment, remaining in solution was precipitated. The pigment, filtered off, dissolved in sodium carbonate solution, but the addition of an excess of hydrochloric acid and saturation with magnesium sulphate failed to yield a precipitate (difference from Mörner's observation). The pigment, however, could be obtained from this solution on the addition of a like volume of 25 per cent. acetic acid.

The pigment was insoluble in water, alcohol and ether. Certain of Mörner's preparations showed a different solubility in acetic acid than is noted below. In judging of such results it must be emphasized that no method has as yet been discovered for isolating the melanin pigments with the help of indifferent chemical agents. It is therefore very probable that uncontrollable changes in structure may occur in the modes of preparation employed which can account for the failure of the observations of various investigators to be in strict accord. Thus it could be ascertained in our case that merely heating the pigment on the water-bath rendered it less soluble in alkali. In general it can, however, be stated that our preparations showed close similarity in their chemical behavior to the urinary and tumor melanin preparations obtained by Mörner.

Analyses of Urinary Pigment. A trace of iron and sulphur was found in the ash.

Ash determination, 0.5006 gm. of water-free pigment yielded 0.0439 gm. incombustible residue. Ash = 8.76 per cent. Determination of nitrogen by Kjeldahl. Preparation I, N = 10.81 per cent. Preparation II, N = 13.15 per cent. Determination of sulphur according to Carius. 0.1599 gm. water-free pigment gave 0.00865 gm. BaSO₄. S = 5.41 per cent. These analyses not calculated ash-free.

³ For comprehensive literature concerning the melanin pigments see: Mörner, K. A. H.: *Ztschr. physiol. Chem.*, 1886-87, xi, 66. Furth, O. v.: *Centralbl. f. Allgem. Path. u. path. Anat.*, 1904, xv, 617. Oppenheimer: *Handbuch d. biochem. Menschen u. d. Tiere*, 1908, i, 743. Poulsen, V.: *Ziegler's Beitr. z. path. Anat.*, 1910, xlviii, 346.

In regard to the value of the analyses it is again to be emphasized that the characteristics of this class of substances are so unfavorable that no claim of absolute chemical purity can be made for our preparations. This is evident from the results of the nitrogen and ash analyses which show considerable variation. Such discrepancies are, however, only to be expected in working with substances of this nature. The preparations are, however, probably as pure as others previously described, judging from the modes of preparation stated. The results of our analyses of the urinary costal and prostatic melanin preparations are compared in the following table with Mörner's analytical data. All of Mörner's analyses are included for reasons stated above. This comparison, if showing some variations, is seen to justify the conclusion that the pigments obtained by both workers are, if not identical, at least fairly closely related in composition.

COMPARISON OF ANALYSES OF MELANIN PIGMENTS.*

	Carbon.	Hydrogen.	Nitrogen.	Sulphur.	Iron.	Ash.
Mörner's preparations . .	55.7	5.9	11.08	4.75	Trace	2.02
	to	to	to	to	to	to
	58.1	8.0	12.30	10.18	(0.03 to 0.2)	9.38
Writer's preparations . .	55.7†	5.7†	11.84‡	5.93‡	Trace‡	7.45†
			to			to
			14.41‡			8.76‡

* Elemental analyses calculated ash-free.

† Preparation from prostatic calculus.

‡ Preparation from urine.

DISCUSSION OF RESULTS. The frequency of the association of ochronosis with alcaptonuria, the presence of joint lesions and characteristics of the urine (darkening on standing, reduction in the absence of glucose of alkaline copper and ammoniacal silver solutions) strongly suggested alcaptonuria as a probable diagnosis in this case. However, carefully executed systematic attempts to isolate homogentisic acid from the urine were uniformly negative. The excretion of a urine which darkens on standing is not specific for alcaptonuria for such cases of melanuria without alcaptonuria have been previously reported. The melanuria of carbolic acid poisoning can also be excluded in the subject of the present studies. In the urine, prostate and ribs, therefore, very probably generally distributed in the body, could be isolated a pigment, found by analyses and chemical characteristics to be related to the protein melanins. The presence of sulphur and iron in this pigment excludes definitely any direct origin from homogentisic acid which contains neither of these elements. On the grounds thus enumerated the diagnosis of alcaptonuria can be excluded.

The reduction of alkaline copper and ammoniacal silver solution is common to various aldehydé substances and is therefore by no means characteristic of homogentisic acid. As alkaline solutions

of the isolated and purified pigment failed to give these reactions they are probably to be ascribed to a chromogen of aldehyde nature. *Owing to these findings and considerations the writer does not consider it in general advisable to accept a positive diagnosis of alcaptonuria in a given case without the isolation of pure homogentisic acid and its proper chemical identification.*

The urinary pigment had the same characteristics as that obtained from the costal cartilages. The pigment in other parts of the organism, so far as its quantity enabled examination, showed no obvious differences from that obtained in the urine and rib cartilages. Evidently but a single melanin was present. This pigment was compared as to its reactions with those described by Mörner for melanin obtained from the urine and tumor of a patient suffering with melanosarcoma. In most characteristics these melanins showed agreement. The analyses made in both cases were also in reasonable accord. These grounds seem sufficient to establish a relationship between the pigment obtained from this case and the tumor melanins which are closely related to protein. It may also be mentioned that such melanins very probably consist of large and complicated molecules for such complex substances as methyl dibutylacetic acid,⁴ xyliton,⁵ and pyridin⁶ have been obtained from them. It would be very difficult to imagine the formation of such complicated bodies from pigment derived from carbohic acid and homogentisic acid which are simple phenol derivatives. This may be regarded as an additional reason for accepting that the *pigment under discussion is to be regarded as of complex nature allied to the protein bodies.*

PATHOGENESIS OF OCHRONOSIS. Including the present case reports from 40 individuals exhibiting the symptom-complex of ochronosis have been published. Three groups of these cases can be readily separated according to their etiology as follows:

1. Ochronosis due to carbohic acid poisoning.
2. Ochronosis due to alcaptonuria.
3. Ochronosis due to other causes than (1) and (2).

In the first group, 9 in number, the coloration has very gradually developed after copious and continued applications of carbohic acid to chronic surgical lesions. The origin of the color is evidently from the poison mentioned, for a certain degree of recovery has been reported to ensue on cessation of the phenol treatment.

Into the second group, ochronosis associated with alcaptonuria, fall somewhat more than half of all cases hitherto described. In our review of these reports it was noted that frequently the diagnosis of alcaptonuria had been based practically solely upon the observation of urine which darkened on standing and exhibited reducing

⁴ Speigler, E.: Beitr. z. chem. Physiol. u. Path., 1903, iv, 40.

⁵ Wolf, H.: Beitr. z. chem. Physiol., 1907, v, 476.

⁶ Furth, O. v., and Jerasulem, E.: Beitr. z. chem. Physiol. u. Path., 1907, x, 131.

properties. The extensive study made in the present case has demonstrated the unreliability of such a diagnosis when it fails of corroboration through the presence in the urine and satisfactory identification of the alcapton body, homogentisic acid. In view of this it seems probable that certain cases hitherto confidently described as alcaptonurics may in reality represent ochronosis without alcaptonuria. The actual number of cases exhibiting ochronosis in company with alcaptonuria where homogentisic acid has been unquestionably identified is but a small fraction of those included under this diagnosis in the literature.

In the third group of cases belong the cases studied by v. Hanseman,⁷ Salkowski⁸ and Langstein.⁹ Alcaptonuria and medicamentation, which could lead to melanuria, were excluded, although certain criticisms can be offered to this work. The same holds true for Hecker and Wolf's¹⁰ patient. As stated a number of apparent alcaptonuric cases are possibly to be included in this category. The present case represents the first of these doubtful cases to be subjected to a thorough chemical study, including isolation of the pigment in a purified state and its analysis. The resulting diagnosis, that of ochronosis unaccompanied by alcaptonuria, though representing nearly a unicum in the literature, may, however, be fairly regarded as placed on a firm basis as a result of this detailed investigation.

On first sight any attempt to reconcile these wide clinical variations to a common cause seems quite hopeless. Why should an extraneously applied poison, as is phenol lead to the identical clinical symptoms as appear in connection with a definite disorder of intermediary metabolism (alcaptonuria) and at the same time be found in other cases quite distinct from either of these conditions? The first insight into the real nature of ochronosis was, however, afforded by Pick,¹¹ who put forward the view that through the action of the oxidative ferment tyrosinase, phenol substances were changed into melanin pigment. Abderhalden and Guggenheim¹² have in recent years materially added to our knowledge of the formation of melanin by the action of this ferment. They found in extended and comprehensive studies that simple phenol compounds, homogentisic acid, the amino acid tyrosin and polypeptids containing tyrosin were all acted upon by tyrosinase, with the resulting formation of melanin pigment. All these substances contain the oxyphenyl group and can be designated by the general formula $R.C_6H_4.OH$, in which

⁷ Berl. klin. Wchnschr., 1892, xxix, No. 27, 660.

⁸ *Ibid.*, p. 661.

⁹ Beitr. z. chem. Physiol. u. Path., 1904, iv, 145; Berl. klin. Wchnschr., 1906, xliii, 597.

¹⁰ Festschr. z. Feier d. fünfzig jährigen Bestehens d. Städt. Krankenhaus zu Dresden-Freiderichstadt, Dresden, 1899, 323.

¹¹ Pick, L.: Berl. klin. Wchnschr., 1906, xliii, 591.

¹² Ztschr. physiol. Chem., 1907-08, liv, 331.

R may represent hydrogen or a complicated group. A peculiar specificity in the action of this ferment could also be demonstrated, inasmuch as it did not effect phenylalanine, the amino acid closely related to tyrosine, nor indeed diiodotyrosin. In phenylalanin and diiodotyrosin the hydroxy group ($-OH$) is absent although the benzene ring is represented in both these substances. The conclusion may therefore be drawn that for the development of pigment by the action of tyrosin the oxyphenyl group $R.C_6H_4.OH$ is necessarily present.

Application of these important studies to the pathogenesis of ochronosis has, however, not yet been made, although they represent the key to a clearer comprehension of the etiology of this condition. From Abderhalden and Guggenheim's studies it may be reasonably presumed that an accumulation of excessive and abnormal amounts of substances within the organism possessing the oxyphenyl group would lead to the production of melanin pigments by ferment action. This seems to be borne out by the clinical observations on carbolic acid poisoning and aleaptonuria, both these substances containing this chemical entity.

In seeking a possible explanation for those obscure cases, including the present one, where both of the above evident causes of the ochronosis fail to be present, the observation of pigment formation from higher compounds such as polypeptids, closely related to protein, becomes of interest. It seems not unlikely from the number and complexity of the split products of such melanins which have been observed that this class of the black pigments may indeed be of very complex constitution. Their tyrosin content may, however, be responsible for the development of the pigmentation owing to the oxyphenyl group contained in this amino acid. The tumor and other protein melanins among which the example here described apparently belongs probably owe their origin to a metabolic anomaly of this nature.

Just how important a part is played by ferments in this pigment formation is, owing to the absence of definite evidence, still a matter of speculation. Still the ferment tyrosinase is now known to be extensively distributed in animals, having been found in the skin and even in melanosarcomata. It is then probable that tyrosinase is normally present in the organism. It seems then fair to assume that the action of this ferment on chromogenic substances such as tyrosin, tyrosin-containing complexes, homogentisic acid, phenol, etc., when present in increased amounts within the body is the ultimate cause of the ochronosis symptom-complex.

Although sulphur and a trace of iron were present in the pigment of this case, this seems no ground for regarding this melanin to be of blood origin. According to von Fürth,¹³ who has extensively

¹³ Fürth, O. v.: Oppenheimer's Handbuch. d. Biochem. Menschen. u. d. Tiere, Jena, 1908, i, 743.

studied the melanins, iron and sulphur groups are to be regarded not as primary in such pigments for which the oxyphenyl group is characteristic. Indeed sulphur is frequently entirely absent or present in an amount much greater than it is represented in hemoglobin which facts preclude of accepting the blood pigments as the mother substances of the melanins.

The Relation of Ochronosis to Alcaptonuria. Ochronosis frequently accompanies alcaptonuria and it may be reasonably assumed from the foregoing considerations that the pigmentation of alcaptonuria is due to a melanin arising from homogentisic acid. This view is accepted by Gross and Allard¹⁴ as follows:

“Die Ochronose und die Alkaptonurie sind Erscheinungen ein und derselben Stoffwechselerkrankung, die klinisch in der Ausscheidung von Homogentisinsäure, der Alkaptonurie und oft in arthritischen Beschwerden, pathologisch-anatomisch in der Ablagerung eines Farbstoffs, der Ochronose, ihren Ausdruck findet.”

Although it is probably true that the ochronosis and alcaptonuria when occurring simultaneously are indeed to be regarded as “expressions of the same metabolic disease,” all cases of ochronosis certainly cannot be properly ascribed to alcapton origin as is the evident opinion of these authors. The nine known cases of ochronosis due to carbolic acid intoxication as well as the others, including the present one, enumerated above where alcaptonuria could be excluded, militate against the acceptance of this theory. It may also be mentioned that in alcaptonurics the signs of ochronosis have been found absent also on postmortem section.¹⁵ The views concerning the pathogenesis of these conditions described in the preceding pages of this article seem sufficiently comprehensive to establish the general relationship of these rare anomalies of metabolism.

RELATION OF THE PHYSICAL SIGNS TO THE ROENTGEN PLATE IN PULMONARY TUBERCULOSIS.¹

By J. J. SINGER, M.D.,

PHYSICIAN-IN-CHARGE, TUBERCULOSIS CLINIC, WASHINGTON UNIVERSITY MEDICAL SCHOOL, ST. LOUIS, MISSOURI.

(From the Department of Internal Medicine, Washington University Medical School.)

THERE has been considerable controversy as to the value of the roentgen-ray findings in reference to the diagnostic benefit in pulmonary tuberculosis. In order to obtain the greatest benefit

¹⁴ Mitt. aus d. Grenzgeb. d. Med. u. Chir., 1908-09, xix, 24.

¹⁵ Fürbringer, P.: Berl. klin. Wchnschr., 1875, xii, 330. Moraczewski, W. v.: Centralbl. f. inn. Med., 1896, xvii, 177.

¹ Read before the St. Louis Medical Society.

from a plate it is absolutely necessary to compare the physical signs with the shadows seen on the plate.

In a broad sense the same factors which alter sound vibrations alter light vibrations. Sound and light are therefore, more or less, of the same character. Light waves, however, travel many times more rapidly than sound waves, consequently the physical signs which constitute variations of sound waves may be correlated with the roentgen plate which gives the variations of light waves. It is the purpose of this paper to discuss the relation of physical signs to the finished plate.

There are a large number of charting schemes, especially one by Sahli, that are in use in various parts of the country, by which anyone familiar with the chart can easily interpret the findings. The method that I use in our clinic is one that I found much simpler than the one in vogue, and one is enabled to interpret the findings in terms of physics:

The scheme is as follows:

MS—muscle spasm.

BS—breath sounds.

WS—whisper sounds.

VS—voice sounds.

VF—vocal fremitus.

TF—tactile fremitus.

++++ —plus represents the degree of increased intensity.

---- —minus represents the degree of decreased intensity.

///// —parallel lines in one direction represent impaired resonance.

—parallel lines in two directions represent dullness.

—parallel lines in three directions represent flatness.

×××× —denotes rales, the character of which is written in the margin.

While this scheme of charting is not perfect it helps to interpret the relation of physical signs in terms of physics.

BS—breath sounds—represent the number of vibrations set up in the chest wall as heard through a stethoscope, and are due to the vibrations set up by the passage of air into the bronchus through the bronchioles and vesicles, altered more or less by the character of the medium through which the sound waves travel.

WS—whisper sounds—represent the waves set up in the chest wall by the whisper, altered, more or less, by the medium through which they travel.

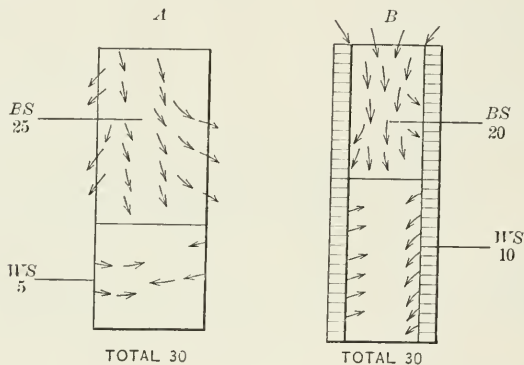
For the sake of convenience I use the symbols *BS* two plus and *WS* one plus and no impairment of resonance as the normal type of breathing (normal vesicular breathing).

In order to demonstrate the theme of the paper I will present the following hypothesis:

Let *A* represent a bronchus or bronchiole, with thin walls over

which one hears thirty vibrations per second on the chest wall, due to the act of taking a deep breath. Let *B* represent a bronchus or bronchiole, with dense or infiltrated walls over which one hears approximately the same number of vibrations. In order to explain the phenomena we must know that sound waves travel indefinitely, although we have no means as yet by which to recognize them as sound beyond a certain distance from their source. The transmission of these waves depends on the density of the substances through which they travel—some substances retard the vibrations while others increase the vibrations by being set in resonance in unison, in this way increasing the number of sound waves.

The Physics of Chart A. Thirty-five vibrations per second are set up by the passage of air into the bronchus—the walls being thin, some of the vibrations will pass on through the wall, leaving twenty-five to be heard over the area while five have been added by the resonance of the thin walls.



The Physics of Chart B. From the same deep breath as taken in Chart A only twenty vibrations could enter the bronchus on account of the thickened walls and none of these twenty could penetrate the dense walls, consequently they were confined—the force, however, has set the walls in resonance, which adds ten vibrations. Thus we have the same number of vibrations over both bronchi but produced by different causes.

A roentgen-ray picture of *A* would show the lines thin and far apart while the picture of *B* would show dense lines with only small air content.

The physical signs of *A* and *B* give one the same mental picture as the roentgen-ray shadows—the one viewed by variation of sound waves while the other by variation in light waves.

It is necessary here to admit that the roentgen ray permits one to recognize differences in light much more easily than the ear

perceives differences in sound; but when one uses the ear and the eye together, with logical deductions, one cannot go very far astray in proper conclusions.

The skiagram is only part of the physical signs of the chest, and to interpret them as having any effect on the patient's condition one must look to symptoms, temperature record, history and other findings.

I will attempt to demonstrate the value of correlating the physical signs with the roentgen plate by describing first the roentgen plate and then the physical signs as elicited by careful examination.

CHART I.—Case 1.

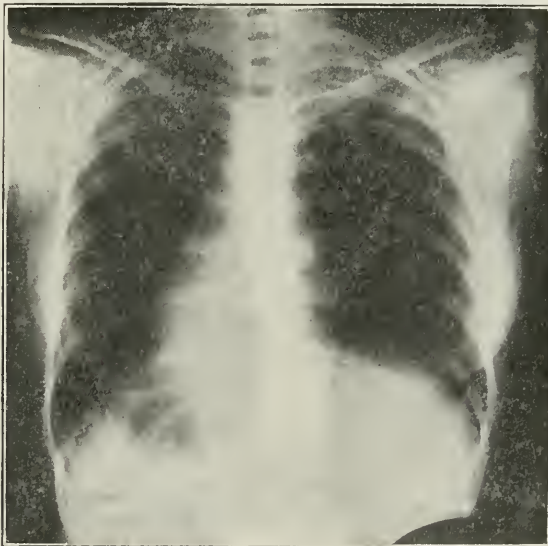
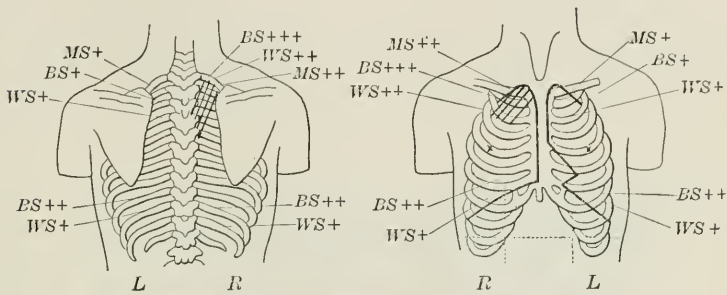


CHART I.—The plate being a flat picture all parts of the chest are in one plane, consequently it is impossible from the picture to interpret whether the shadows seen are anterior or posterior, but the physical signs show where one can put the shadows in their proper relation even without a stereoscopic picture.

The right upper: One sees a thickening of the interlobular lines and moderate approximation and interlacing. Here and there air-containing spaces are noted. The lines in the lower lobe are distinct, not thickened, and there is considerable air-containing spaces. The diaphragm on the right side is rounded and the costal angle is deep. In the left chest, upper portion, there is a moderate thickening of the interlobular lines, with no approximation. The air content is good. In the lower lobe the lines are not thickened. The diaphragm is rounded and the costal angle is deep.

PHYSICAL SIGNS. Anterior on the right we have impaired resonance and two-plus muscle spasm. The breath sounds are harsh and whispered sound is increased. In the lower lobe the breath sounds are normal as well as the whisper, with no impairment of resonance. The left chest, upper part, muscle spasm, one plus. The breath sounds are relatively diminished and the whisper is normal, with no impairment of resonance. In the lower part, anterior, the breath sounds are normal, two plus, whispered sound one plus, with no impairment of resonance.

Posterior, right upper, muscle spasm is two plus, breath sounds three plus, whispered sound two plus and resonance is impaired. Lower part is normal—breath sounds two plus and whisper sound one plus. Posterior, left upper, muscle spasm one plus, breath sounds one plus, whispered sound one plus, with no impairment of resonance noticeable. Lower left is normal: breath sounds two plus, whispered sound one plus.

Correlating the physical signs with the shadows seen on the roentgen plate we must come to the same conclusion in the light of the physics of sound and light. The physical signs in the right upper, anterior and posterior, shows a three-plus breath sound and a two-plus whisper, with an impairment of resonance, a syndrome, as it were, which could only be produced by a moderate infiltration of the tissues in which were air-containing spaces. The increase in whisper demonstrates that the walls of the tubes are thickened and have added more vibrations to the breath sounds as explained in Fig. B. If the walls are thickened we can readily understand the impairment of resonance as found by percussion. In the plate the interlobular lines are thickened and approximated, a condition producing a shadow in which the air content is small and proves that only a small amount of air-borne vibrations are taken in the lung. The muscle spasm over the right upper, anterior and posterior, is more marked on the right than on the left, which condition is interpreted as activity. In the left upper part of the chest plate we see a moderate thickening of the interlobular lines, but with considerable air space, a condition noted by physical signs by the diminished breathing, with no impairment of resonance. The lower part of both lungs in the plate shows the lines far apart and not thickened, with considerable air space. A like interpretation was given to the physical signs, denoted by breath sounds two

plus, whisper one plus. We see here an agreement of physical signs and roentgen-ray plate, but the plate gives a more graphic picture of actual lung condition, and one feels much surer of his findings when the variation of sound waves demonstrated by physical examination is verified by the roentgen plate.

CHART II.—Case 2.

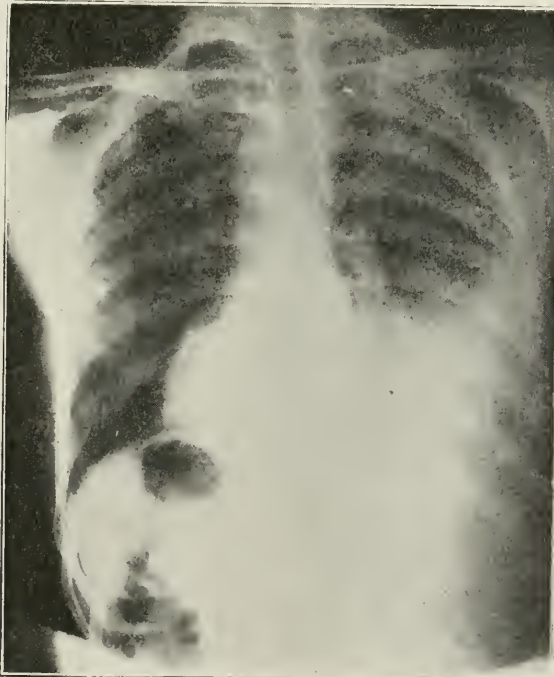
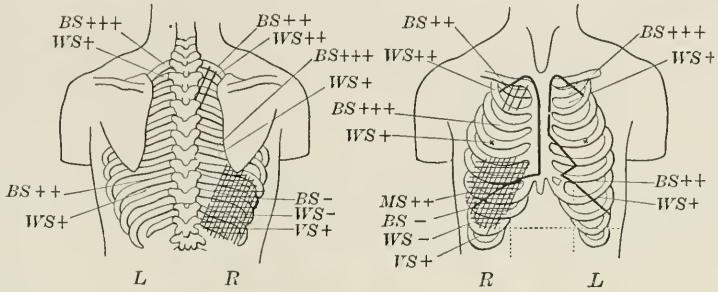


CHART II.—Air content good in the left lung. The hilus is fairly dense, with a few small nodules. Interlobular lines visible, but not approximated or thickened. The costal angle is deep. On the right, upper portion, the interlobular lines somewhat thickened and very closely approximated, especially in the upper portion, while

below this the lines are indistinct and there is considerable air space. The hilus is compressed. A homogeneous shadow extends from the seventh posterior rib and shades into the shadow of the liver. Shadow of the diaphragm not visible. No costal angle seen.

PHYSICAL SIGNS. CASE 2. Anterior on the left we have loud breath sounds three plus, whisper one plus, and hyperresonance. The lower portion, breath sounds and whisper normal. On the right, anterior, there is an impairment of resonance in the upper part, with normal breath sounds, but the whisper is increased, two plus. From the second to the fifth rib we have an area of increased breath sounds three plus, with whisper one plus, compensatory emphysema. From the fifth rib to the last rib there is an area of flatness, with muscle spasm marked, two plus, breath sounds and whisper sounds not heard and the voice sound barely transmitted.

Posterior on the left similar to anterior, while on the right the flatness begins at the seventh rib.

Correlation of Physical Signs and Roentgen Plate. The physical signs show an impairment of resonance in the right upper, anterior and posterior, with increased whispered sounds and no noticeable increase in breath sounds, a condition which indicates an area of lung in which there is less air than normal, the two-plus whisper indicating a congestion or compression of the lung tissue. In the plate we find the interlobular lines closely approximated, not thickened, a condition which definitely shows that less air was in that part of the lung. The hyperresonant area indicated on the chart is demonstrated on the plate by the "brilliant" condition, which shows that a great deal of air was in that part of the lung.

The flatness seen in the lower part of the lung shows by the diminished breath and whispered sounds that no air was in that part of the lung (lost by diffusion of vibrations). The shadow seen on the plate, being homogeneous, shows a like condition, that is, no lung tissue in that area. The compression of the hilus demonstrates that the entire lung is compressed from below.

We again see here an agreement of the physics of light and sound. The condition was diagnosed pleural effusion and was proved by thoracentesis.

CONCLUSIONS. 1. It is possible in most cases to predict the roentgen findings after a careful physical examination has been made.

2. One can show by charting the physical signs as indicated in the paper in terms of physics.

3. Every available means should be used to assist us before interpreting conditions hidden from our sight before hazarding a definite diagnosis.

4. The shadows seen on the roentgen plate is only a physical sign.

NOTE.—Unfortunately a print of a roentgen plate does not bring out the finer lines, consequently the demonstration of the prints is not as conclusive as one would like.

A CASE OF CONGENITAL ABSENCE OF THE UTERUS WITH ANOMALOUS VULVOVAGINAL ANUS.

BY E. J. STRICK, M.D.,

CHICAGO, ILLINOIS.

IN May, 1915, a Chinese girl, aged twenty years, entered the Wilhelmina Hospital, Amoy, China, with the complaint that her menstrual flow came from the urethra instead of from the vagina. The patient was extremely timid, and her mother had to state her case.

Upon external examination it was found that the pubic hairs were scant, but this is usual among the Chinese. There was a complete absence of anal opening at the usual site. Clitoris, labia and urethra were normal. The vaginal opening was rather small, and there was no trace of a hymen.

Upon internal examination no uterus could be felt, but one could feel a broad band in the pelvis stretching from side to side, and sagging somewhat in the middle. On the right side near the pelvic brim there was in this band a small gland-like object, about 2 cm. in diameter. No gland was palpable on the left side. On examining the posterior part of the cavity it was found to be very roomy. There was no septum dividing the vagina from the rectum. The examining finger came in direct contact with feces in the rectum. By introducing a sound into the bladder and two fingers into the rectovaginal cavity no uterus could be felt. The bladder seemed to be without defect. By the aid of a speculum our previous findings were confirmed and no further trace of a uterus could be found.

The patient's breasts were normally developed and she had a normal feminine voice and appearance. She was kept under observation in the hospital for about two months to determine whether we were probably dealing with a case of vicarious menstruation. But during that time no signs of menses appeared.

These findings were confirmed by J. Henderson Lamb, M.B. (Edin.), of Chang-poo, China, and Miss W. Murman, accoucheuse (Amsterdam), and head nurse in the Wilhelmina Hospital, Amoy, China.

Absence of the uterus is considered sufficiently rare to merit report. That it is not as rare as earlier writers have believed is shown by the increase of the number of cases reported in recent literature. From time to time there have been attempts to collect and classify the cases that have been described. Among the earlier attempts were those of Thudicum,¹ Fürst² and Kussmaul.³ In

¹ Monatsch. f. Geburtsh. und Frauenkr., Berlin, 1855, v, 272-289.

² Ibid., 1867, xxx, 119; 161.

³ Von dem Mangel, der Verkümmerng und Verdopplung der Gebärmutter, 1859, Würzburg.

1897 Burrage⁴ reviewed the literature and collected 360 cases reported by 239 different writers.

Since the review by Burrage, 76 cases have been reported by 66 different writers. This includes those of 1896, since they were probably not included in the previous review. In only 51 cases was the literature accessible. The only data obtainable in the others were from what appears in the titles of the articles.

Of the 51 cases in which the literature was accessible, 1 was diagnosed at autopsy, 1 was found during dissection and 7 were confirmed by abdominal operation. The others were diagnosed in the living subject. Such a diagnosis is not always reliable, since bands of muscle may be present which morphologically represent the uterus but which cannot be detected by ordinary methods of examination. But for practical purposes we may accept such diagnoses.

Burrage finds that the absence of ovaries in conjunction with absence of the uterus is exceedingly rare. Previous to 1897 there were only 6 cases on record, and in only 3 was the diagnosis verified postmortem. Since then 26 such cases have been reported. The case of Sloan⁵ was discovered at autopsy and the case of Forbes⁶ during dissection. In the case of Lynds⁷ an operation was performed and no ovaries were found, but by microscopic examination of the tumor which was removed, Warthin discovered a rudimentary ovary.

The absence of tubes in cases of congenital absence of the uterus is equally rare. Burrage reported 6 cases, of which only 1 was confirmed at autopsy. We found 18 cases reported in recent literature, 4 of which we must accept without question, viz., those of Sloan, Forbes, Lynds and Van Bockstaele.⁸ Borelius⁹ and Smith¹⁰ each reported a case in which there was absence of only one tube and one ovary. Both of these cases were confirmed by operation.

Among the 76 cases there were only 3 in which the ovaries (or in one case perhaps the testes) were found in the inguinal canal. These were the cases of Gillmore,¹¹ Swasey¹² and Cullen.¹³ English¹⁴ previously reported 38 cases of ovarian hernia, of which 27 were inguinal.

It has been said that in the majority of cases of absence of the uterus there is also absence of the vagina or a rudimentary develop-

⁴ AM. JOUR. MED. SC., 1897, n. s., cxiii, 310-321.

⁵ Phil. Med. Council, 1896, i, 140.

⁶ Montreal Med. Jour., 1901, xxx, 848.

⁷ Jour. Mich. Med. Soc., Detroit, 1905, iv, 122.

⁸ Jour. Méd. de Brux., 1913, xviii, Supplément 91.

⁹ Hygiea, Stockholm, 1896, lviii, pt. 2, 190-192.

¹⁰ Ann. Gyn. and Pediat., Boston, 1905, xviii, 169-172.

¹¹ Am. Jour. Obst., New York, 1906, liii, 520-525.

¹² Am. Med., Philadelphia and New York, 1907, n. s., ii, 519-521.

¹³ Surg., Gyn. and Obst., Chicago, 1910, xi, 73-75.

¹⁴ Jahrbuch. der K.-K. Gesellschaft der Aerzte in Wien. 1871.

ment of the same. We have found that there were 29 cases of absence of the vagina and 20 cases of rudimentary development. This forms more than 60 per cent. of the total number.

In all the literature on this subject we have been able to find only 3 cases in adults in which an anomalous vulvovaginal anus was associated with congenital absence of the uterus, viz., those of McCann,¹⁵ Bullard¹⁶ and Lurier.¹⁷ Bosquet,¹⁸ in 1757, mentions the case of an infant, which died at birth, in which there was a persistent cloaca, absence of the uterus and absence of the bladder. There may have been other cases in monstrosities, but the above mentioned are the only ones reported in adults.

In McCann's case there was a rudimentary uterus present, but the rectovaginal septum was incomplete. Bullard's findings are briefly as follows: The external genitalia were normal; there was no evidence of a uterus; there was a fibrous band extending from one side of the pelvis to the other; the ovaries seemed to be present but small; there was no normal anus but the rectum communicated with the upper end of the vagina about 2.5 or 3 cm. from the ostium, and at this point there seemed to be an annular constriction resembling a sphincter ani. In Lurier's case there was an absence of the uterus and vagina and the anus was found in the usual position of the vagina, opening below the fossa navicularis. There was a horizontal band between the rectum and the bladder, which Lurier considers might probably be a rudimentary uterus.

Although absence of the uterus is considered rare the occurrence of an anomalous vulvovaginal anus is much more rare. Von Bardeleben¹⁹ estimates that there is one such case in every 25,000 or 30,000 births. In the cases mentioned above and in the one just reported there has been a failure in the development of the septum which separates the urogenital sinus from the rectum as well as a failure in the development of the Müllerian ducts. It is not necessary to enter into a discussion of the development of the genitalia or of the rectovaginal septum, since this has been thoroughly covered in recent articles. We have merely given a general survey of the recent literature on the subject of absence of the uterus and have grouped the few cases which, like the one just reported, have an associated anomalous vulvovaginal anus.

¹⁵ AM. JOUR. MED. SC., 1896, n. s., cxii, 393.

¹⁶ Jour. Am. Med. Assn., 1898, xxxi, 479.

¹⁷ Deutsch. med. Ztg., Berlin, 1904, xxv.

¹⁸ Recueil périodique d'observations de Méd. Chir. et Phar. ou Jour. de Méd., vi, 128, 1757.

¹⁹ Arch. f. Gynäk., Berlin, 1903, lxxviii, 3-56.

REFERENCES.

1. Leech, J. W.: *British Med. Jour.*, London, 1896, ii, 1035.
2. Milne, L. J.: *Ibidem*, 1901, ii, 981.
3. Bell, C. E.: *Ibidem*, 1904, ii, 1751.
4. Bell, R. H.: *Ibidem*, 1904, ii, 1571.
5. Paramore, R. H.: *Ibidem*, 1905, i, 302.
6. Rose, E. N. MacB.: *Ibidem*, 1908, ii, 1224.
7. Sorabji, Alice M.: *Lancet*, London, 1906, ii, 160.
8. Boston, L. N.: *Ibidem*, 1907, i, 21.
9. Brown, A.: *Ibidem*, 1909, i, 1456.
10. Naylor, H. G. H.: *Australian Med. Gaz.*, Sydney, 1899, xviii, 453.
11. Hamilton, A. F.: *Indian Med. Gaz.*, Bombay, 1910, xlv, 57.
12. Hedley, J. P.: *Jour. Obst. and Gyn. British Empire*, 1911, xx, 186-188.
13. Müllerheim: *Ztsch. f. Geburtsh. und Gyn.*, Stuttgart, 1898, xxxviii.
14. Palm: *Zentralbl. f. Gyn.*, Leipzig, 1906, xxx, 878.
15. Dalché, P., and Malbec, A.: *Gynéc.*, Paris, 1908, xii, 139-141.
16. Ladinski, L. J.: *Am. Jour. Obst.*, New York, 1898, xxxviii, 78-85.
17. Wright, E. S.: *Ibidem*, 1899, xxxix, 184.
18. Brettauer: *Ibidem*, 1907, lvi, 867-868.
19. Fränkel, M.: *Ibidem*, 1910, lxii, 485.
20. Dorland, W. A. N.: *Am. Gyn.*, New York, 1903, ii, 346-351.
21. Corson, E. S.: *Philadelphia Med. Jour.*, 1903, xi, 538.
22. Shipps, W. H.: *Ibidem*, 1903, xi, 653.
23. Bustillo-Lirola, A.: *Ann. Gyn. and Pediat.*, Boston, 1902, xv, 731.
24. Carson, N. B.: *Tr. Am. Surg. Assn.*, Philadelphia, 1900, xviii, 339.
25. James, J. A. and T. H.: *Med. News*, New York, 1899, lxxv, 20.
26. Fisher, C. E.: *Homeop. Jour. Obst.*, New York, 1902, xxiv, 9-15.
27. Wathen, W. H.: *Louisville Med. Monthly*, 1896-7, 370-372.
28. Spruill, J. L.: *North Carolina Med. Jour.*, 1896, xxxviii, 359-364.
29. Harlan, E.: *Cincinnati Lancet-Clinic*, 1902, n. s., xlvi, 87.
30. Barker, G. G.: *Med. Sentinel*, Portland, Ore., 1902, x, 574.
31. Robinson, E. M.: *Alabama Med. Jour.*, Birmingham, 1905-6, xviii, 513.
32. Kalizionis, E.: *Bull. et mém. Soc. de chir. de Paris*, 1911, xxxvii, 710.

CLINICAL EXPERIENCE WITH KOGA'S CYANOCUPROL.

BY T. I. MASUDA, M.D.,

ISHIGAMI HOSPITAL, TENNOJI, OSAKA,

AND

T. K. MATSUDA, M.D.,

ISHIGAMI SANITARUM FOR CONSUMPTIVES, HAMADERA, NEAR OSAKA.

THE problem of tuberculosis therapy is one of the most absorbing and elusive in medicine. Koch's epoch-making invention of tuberculin was accepted at first with the greatest interest not only by the medical profession, but by those who were suffering from the disease. Its therapeutic value, however, was not as great as anticipated, while, on the other hand, so many disadvantages were detected in the form of so-called reactions that it finally came to be considered not only useless but actually injurious, and its clinical application was practically given up. Subsequently many improvements were attempted by Koch himself and many others until more than forty preparations have been reported, none of which seems to be either efficacious or entirely free from harmful reactions.

Since Ehrlich and Hata obtained such brilliant success in the treatment of syphilis with salvarsan many attempts have been made to discover a remedy for the treatment of tuberculosis on similar principles. In April of last year, at the annual meeting of Kenkyusho Dosokwae (Association of the Fellowship of Kitasato Institute for Medical Research), Dr. Koga read a paper reporting the success in animal tests as well as in the clinical application of his own antituberculosis remedy. The new preparation, which has been named cyanocuprol, is the compound salt of potassium cyanide with copper (as may easily be inferred from the name), the exact chemical composition of which has not yet been reported. He began his experiments with potassium cyanide, and he found that in some animals its use resulted in a distinct healing tendency. In most cases, however, the destructive process was most evident because of the strong toxicity of the drug. He experimented further, trying to prepare some other compound which would be more effective and less poisonous. The new preparation which he succeeded at last in making was suggested by Koch's "aurum kalii cyanatum" and Linden's copper compound. After several series of animal tests, he concluded:

1. That guinea-pigs previously inoculated with tubercle bacilli and then treated with this preparation do not die of the infection or at least their lives are prolonged in comparison with the control animals.

2. That the drug has considerable healing ability, as shown by the condition of the affected organs at autopsy and by subsequent histological study. There is marked influence in the stimulation of formation of new tissue from surrounding parts, and the tubercle bacilli contained in them are in some instances entirely killed. Inoculations with pieces of such organs into healthy animals cause no tuberculous process.

3. That the injection of the drug, if begun at the time of inoculation or within four days from it, does not prevent the onset of tuberculosis. After the formation of nodular tubercles, however, it begins to manifest its influence upon them.

4. That some signs of reaction are constantly observed after the injection in the form of local hyperemia and infiltration of round cells, followed finally by proliferation of fibroid tissue (encapsulation).

5. That too large doses are distinctly harmful, because a softening of the tubercles and a generalization of the process is caused and the animal dies.

From the foregoing statements we may assume that the preparation is by no means germicidal, except in a secondary way. It shows little parasitropic nature, while the organotropic property seems to be great, and so it may not be called a strictly chemotherapeutic remedy, according to Ehrlich's definition. Yet a favorable influence is experimentally proved with certainty.

Koga proceeded further to apply this remedy to 125 patients. The results are shown in the following table:

	Number of patients.	Cured. ¹	Improved. ²	Died.	Treatment discontinued.	In course of treatment.
Passive cases:						
1st stage . . .	19	13	2	0	1	3
2d stage . . .	6	3	3	0	0	0
3d stage . . .	4	1	3	0	0	0
Active cases:						
1st stage . . .	7	4	2	0	0	1
2d stage . . .	11	3	5	0	1	2
3d stage . . .	8	0	3	3	0	2
Surgical tuberculosis	8	1	4	0	2	1
Total . . .	63	25	22	3	4	9

LOCAL REACTIONS. On the day after injection a slight dulness and rales appeared over the affected spot, where no such physical symptoms were evident before the injection, or if such signs were present, they increased in degree and extension. In from seven to nine days the reactions disappear.

In cases of skin tuberculosis the affected parts become reddened and swollen, painful to pressure, and sometimes suppurative. After ten days this reaction entirely disappears. In 5 cases of glandular tuberculosis the swollen glands became painful and the swelling increased. The pain and swelling gradually decreased after five days until the glands were somewhat smaller than before. On the next injection they again became painful and swollen, but less intensely than before, and after from five to seven injections they were completely absorbed. In 1 case the suppurating gland broke through to the surface of the skin, but healed without leaving behind a fistula. In 1 case of renal tuberculosis the kidney became swollen and painful, hematuria followed on the day after injection, and the general condition became worse, but in seven days all symptoms gradually decreased. The pain at the time of urination diminished and the turbid urine became clear and transparent.

All of these reactions were much less intense in patients who had been treated previously with tuberculin.

TUBERCLE BACILLI IN SPUTUM. Of 8 patients of the second and third stages the sputum was examined every day, with the following result: From the day after injection the number of bacilli was gradually increased, reaching the maximum point on the fourth or sixth day, when it began slowly to decrease. After from seven to ten days the number was obviously smaller than before the injection, and after repeated injections the bacilli disappeared

¹ Body temperature constantly below 37° C. Absence of clinical symptoms. Patients are able to go on with their work without trouble.

² Symptoms much reduced but not entirely absent.

entirely in favorable cases. Morphologically the bacillus undergoes striking change. In one to three days after the injection the coloring of some bacilli became fainter and homogenized, granular construction was lost, and some were cut into pieces and in appearance resembled streptococci or staphylococci.

FEVER. In some cases, at the first and second injections, the temperature rose to 38° to 40° C. after several hours, then fell gradually to normal in three to seven days. Among 10 highly feverish patients 3 became afebrile after the first injection, 3 after the second, and 3 after the third, while 1 case was entirely unaffected. In all other cases no influence was evident.

BODY WEIGHT. In most cases the body weight decreased (500 grams or more) immediately after the injection, only to be almost restored in a few days or in two weeks at the latest. In exceptional cases the body weight increased a little after the first injection.

SUBJECTIVE SYMPTOMS. Cough and expectoration are usually relieved after the injection and the patient feels fairly comfortable.

ACCESSORY ILL EFFECTS. No remarkable symptoms may be noticed as accessory ill effects of the remedy itself. Sometimes if the solution is injected too rapidly the patients complain of an uncomfortable feeling on the chest and of palpitation of the heart immediately after the injection. In most cases night-sweats are complained of for two or three days after the injection.

DOSES. As shown in the animal experiments too large doses are injurious. The doses suggested by Koga are as follows:

For incipient cases, 7 to 9 c.c.

For advanced cases, 6 to 7 c.c.

Doses should be given intravenously and repeated five to ten times at intervals of two weeks or more. This interval was proved most satisfactory by animal tests. It should never be shortened.

CONTRA-INDICATION. The treatment is contra-indicated for those in whom the respiratory surfaces are too much affected or the general condition too seriously weakened.

EFFECT OF OTHER DRUGS ADMINISTERED DURING TIME OF TREATMENT. Aq. lauroc., creosote, guaiacol, and iodine preparations should not be used during treatment with cyanocuprol.

Koga's paper was received with great interest. He was unwilling, however, to offer the remedy immediately for public use, but felt that it should be tested further on the sick bed, not only by himself but by many other skilled practitioners, in order that an impartial estimate might be made of its therapeutic value and that the details of its practical application might be thoroughly worked out. For the purpose of this investigation twenty well-known hospitals and sanatoria were asked, in the name of Prof. Kitasato, the president of the institute, to try this preparation on the sick bed. Accordingly, we began to use it in May, 1915, and up to the end of 1915 about two hundred patients had been treated. We

collect here a record of the experiments of this period and will report the general result. Of course this period of half a year is too short to make any definite statement, especially with regard to the therapeutic value of a preparation for a chronic disease like tuberculosis, the total course of which may extend over several years. What is said here, therefore, is necessarily of temporary validity. Whether this result may be of ultimate value can be decided only by further observations.

We may summarize the total results in the following table:

TOTAL NUMBER OF PATIENTS TREATED.

	At Tennoji.	At Hamadera.
1st stage	17	21
2d stage	36	57
3d stage	23	29
	76	107

TOTAL RESULTS OF THE TREATMENT.

AT TENNOJI.

	1st stage.		2d stage.		3d stage.		Total.	
	No. of patients.	Per cent.	No. of patients.	Per cent.	No. of patients.	Per cent.	No. of patients.	Per cent.
Cured	10	58.8	9	25.0	0	0	19	25.0
Much improved	6	35.3	20	55.5	6	26.1	32	41.2
Somewhat improved	1	5.9	5	13.9	14	60.9	20	26.4
Remaining unchanged	0	0	0	0	2	8.7	2	2.6
Worse	0	0	1	2.8	1	4.3	2	2.6
Treatment discontinued	0	0	1	2.8	0	0	1	1.3
	17	..	36	..	23	..	76	

AT HAMADERA.

	1st stage.		2d stage.		3d stage.		Total.	
	No. of patients.	Per cent.	No. of patients.	Per cent.	No. of patients.	Per cent.	No. of patients.	Per cent.
Cured	16	76.4	9	15.8	0	0	25	23.4
Much improved	4	19.1	28	49.1	4	13.8	36	33.7
Somewhat improved	1	4.8	16	28.7	19	65.5	36	33.7
Remaining unchanged	0	0	1	3.5	3	10.3	4	3.7
Worse	0	0	0	0	2	6.9	2	1.8
Treatment discontinued	0	0	3	5.4	1	3.4	4	3.7
	21	..	57	..	29	..	107	

The stage is decided upon by a comparison with the standard given by the Bureau of Hygiene of Germany.

Cured: No fever, objective and subjective symptoms absent, and patients are able to go on with their work without feeling any inconvenience. No bacilli found in the sputum.

Much improved: Only slight objective symptoms remain. Patients subjectively quite well. Sputum may contain bacilli.

Somewhat improved: Subjective disturbance diminished. Objective symptoms somewhat reduced. Fever may continue.

Worse: Objective symptoms become noticeably worse after injection, or subjective symptoms seemed aggravated. These may not necessarily have been the direct result of the injection.

NECESSARY PRECAUTIONS BEFORE INJECTION. As the toxicity of the remedy is very great it is absolutely necessary to have the patients under constant observation and control, and consequently they should be treated in hospitals only. Good results could never be obtained, we are sure, with ambulant treatment, for many serious and unexpected accidents may occur, especially when patients have a tendency to hemoptysis. In the case of patients suspected of intestinal tuberculosis, special attention should be paid to the evacuation of the bowels in order to avoid violent reaction. To secure complete and regular evacuations we used magnesium sulphuricum or some other like saline laxatives. Enemas were also used.

TREATMENT AFTER THE INJECTION. At first we required of all patients absolute rest for three days and nights after the injection, according to the instructions of Koga, but as this was sometimes quite unendurable, especially by those who had no very marked symptoms, we afterward changed the requirement to twenty-four hours of absolute rest, allowing them to sit up in bed during the following forty-eight hours at the time of meals and during urination and defecation. No ill effects followed this practice. This is only a general rule, however, and should be properly modified according to the condition of the individual patient. It is best to require during the three-day period, however, a half-fluid diet (rice mush), in order to avoid the irritating reaction in the bowels which very often takes place, especially in cases of intestinal tuberculosis or in patients who have chronic digestive disturbances.

DOSES. The amount injected must, of course, be regulated according to the condition of the patients, but in general we used far smaller doses than those employed by Koga. At first we gave exactly as much as prescribed, but after some experience we found the dose too great and reduced it, and since then various unpleasant reactive phenomena, which formerly had been frequent, have usually been avoided. The doses which we used are as follows:

For patients in the first stage, 5 to 6.5 c.c.

For patients in the second stage, 3 to 4 c.c.

For patients in the third stage, 2 to 3 c.c.

Special attention was given to dosage in cases which gave a his-

tory of repeated or recent hemoptysis. In such cases, even if they were not much advanced, 2 to 3 c.c. were usually given as the first dose, and the amount given at further injections was determined in accordance with the observed effects of this amount. When suitable doses were found the same were kept constant for some time. We found that we had to be very cautious in using increasing doses of the drug, just as with tuberculin, in order to avoid such unpleasant events as hemoptysis, which may take place on the third to fifth injection. At any rate it is absolutely necessary to take into careful consideration the individual constitution and the stage of progress of the disease in each patient and having determined the most suitable dose to continue it throughout the treatment. If the chief symptoms have almost disappeared it is sometimes well to reduce the quantity in the two or three last injections. Otherwise the symptoms may be aggravated rather than entirely removed.

LOCAL REACTION. According to Koga's report the local reaction is more or less noticeable after every injection. Dulness and rales may increase both in intensity and extent. This reaction is proportionate to the healing effect to some extent, *i. e.*, the greater the reaction the greater the healing effect. We first thought, therefore, that the reaction was a manifestation of the healing process, and that consequently that dose should be given which would cause some definite reaction. We found afterward, however, that the healing process and the reaction did not always go hand in hand, and that, on the contrary, the greatest healing effect was accompanied by the least reaction. Therefore we reduced the size of the doses so that the reaction might be avoided as nearly as possible.

As typical reactive symptoms we may count the following signs: On the first or second day after the injection the increase of rales is more or less marked, accompanied by cough and expectoration. At first, when larger doses were given, this exaggeration of symptoms was present at almost every injection, but even at that time the increase of dulness was not always noted, as recorded in Koga's report. With the reduction of dosage this reaction is wanting in most cases. Sometimes the multiple rales, which persisted against all treatments, disappear at once, the dulness is wonderfully lessened, becoming somewhat tympanitic in tone, and the breath sounds become bronchial. These no doubt show that pneumonia-like changes are taking place. It is noteworthy that sometimes at the spot where dulness existed tympany appears and persists for one or two days while all other symptoms remain quite unchanged.

These reactive signs come out in a great majority of cases on the day after injection, and only in rarer cases on the second and third days. Sometimes they may occur only after from five to seven days, and in such cases the result seems generally to be bad. They

do not persist for more than two or three days and are removed usually by keeping the patients at rest without giving any special treatment. At times we obtained a marked sedative effect by the intravenous injection of calcium chloride, 5 per cent. solution. In general the reaction is more marked with large doses and more striking in the more advanced cases.

It is possible that the remedy may stimulate or arrest the process according to the severity of the disease perhaps or the size of the dose. But as there can be no reason that the same agent may have on the same organ or tissue at the same time two quite opposite effects so this apparent paradox should be explained. What seems to be inhibitive is not actually so, but the original effect is of a stimulating nature. When the dose is too small the effect of stimulation lasts for a very short time and soon runs into a period of arrest. Koga's assumption that the reaction itself is the manifestation of the healing process is supported by this explanation. It seems then that the secret of success with this treatment lies in choosing the most efficient dose, which varies with every individual. In this respect the remedy bears a great resemblance to tuberculin.

After the first period of stimulation, at the beginning of the period of arrest, all reactive symptoms become less marked, and the preëxisting dulness, rales, etc., are diminished in most cases. Especially is this true in relatively early cases, when dulness and rales disappear, expiration is no longer prolonged, and in areas in which the breath sounds had weakened or totally vanished, they may be heard again only after two or three successive injections. The disappearance of the dulness is most noteworthy. An effect so marked and so immediate has not been observed with any other remedy. In chronic cases, on the other hand, it is specially difficult to effect a total disappearance of the dulness.

We have avoided injecting patients who are suffering from early pleuritis, fearing that a violent reaction such as Koga described might possibly follow. In chronic cases of pleuritis, however, we have seen the pain and friction rub come out again, or the whole inflammatory process become active, accompanied by fever, pain, and renewed accumulation of exudation, etc. But this was found only in a few cases. In the great majority of cases no marked effect was observed.

INTESTINAL TUBERCULOSIS. It is a well-known fact that cyan preparations possess great affinity for the bowels, and bleeding and submucous hemorrhage have often been observed in animals treated with cyan compounds. Clinical experience corresponds with these observations. Even if the bowel contents were carefully washed out as prescribed, and all possible means used to lessen the reaction, we found patients with intestinal tuberculosis who complained of uncomfortable feeling in the bowels, peristaltic unrest and pain, etc.,

after the injection. At Hamadera one patient discharged a bloody and mucous stool (dysenteric) after the injection. Recovery from this condition was very slow. These reactions may be avoided to a certain extent by evacuating the intestines, as emphatically recommended by Dr. Otani (chief of the clinical department of Kitasato Institute), and by giving smaller doses.

In one case of intestinal tuberculosis we saw a paroxysm of severe gastralgia after every injection, with no particular change in the stool. Another case of gastralgia came on a few hours after the injection in a patient who disobeyed our orders and ate an ordinary meal of boiled rice and some pieces of persimmons. As the patient had complained at two preceding injections of oppression of the stomach this attack of gastralgia may be explained as irritation caused by the injection and aggravated by the alimentary stimulation. The example goes to show how important it is to pay special attention to the diet. The same caution should be used in cases of simple bowel catarrh of acute or chronic nature. We saw several patients with chronic gastric catarrh, dilatation of the stomach, and gastroptosis who felt the stomach oppressed and filled up.

From the foregoing observations we conclude that attention to dosage, evacuation of bowels, and diet (fluid or semifluid diet is necessary) are particularly important in the treatment of patients suffering from intestinal tuberculosis or from general stomach or intestinal disturbances.

GLANDULAR TUBERCULOSIS. The remedy manifests a wonderful effect on relatively early cases of glandular tuberculosis. In cases of lymphoma colli tuberculosum the swollen glands are at first still more swollen and the skin at the point of swelling is reddened; but in a few days these signs diminish gradually, and by the time of the next injection the glands usually have become somewhat smaller than before the treatment was begun. After the next injection they are again swollen, but less extensively so, and as the symptoms abate the glands show further contraction. After several treatments the glands were almost wholly absorbed. A patient at Hamadera may be cited as an example of typical reaction to the treatment. The swollen glands, originally as large as an egg, were almost totally absorbed after six successive injections.

It is important to say here that a somewhat larger dosage is necessary in the treatment of glandular tuberculosis. A patient at Osaka who had a marked lesion in the right lung, which extended through two whole lobes and swollen glands as large as dove's eggs on both sides of the neck, showed a remarkable improvement after three injections, the following doses being given: 4 c.c. at the first injection, 5 c.c. at the second, and 6 c.c. at the third. The multiple rales were wonderfully reduced, dulness almost disappeared, fever descended, and the body weight increased, while not the slightest

influence could be detected on the swollen glands. After the fourth injection, when 7 c.c. were given, the glands became somewhat swollen, became painful to pressure, and were somewhat softened. On the fifth injection (6.5 c.c.), the same reactive signs were definitely noted, but as the pulmonary symptoms, which had practically disappeared, reappeared, the dose was reduced to 5 c.c., and this time no effect was observed. Since then, in spite of three successive injections, the glands remain quite unchanged. From this we may assume that it needs more than 6.5 c.c. to produce a beneficial effect upon glandular tuberculosis.

LARYNGEAL TUBERCULOSIS. Unfortunately the remedy seems to have very little effect on laryngeal tuberculosis.

GENERAL REACTIONS. *Fever.* The influence of the remedy upon fever varies very much, but in most afebrile cases without complication there is no rise in temperature. Occasionally a slight rise (0.5° C.) was observed, which disappeared usually on the following day. In slightly feverish cases the fever disappears in two or three days after injection. The temperature begins to rise before the next injection, which causes it again to fall. Repetition of the treatment brought a permanent afebrile condition after several injections. In favorable cases this result may be obtained by only one injection. We had little experience with highly feverish patients because we tried usually to bring the temperature down near normal, before beginning the treatment, by means of Ishigami's anti-tuberculous serum, autovaccine cultivated from the sputum of the patient, or antipyretics. So far as our experience goes, however, the temperature is sooner or later brought down to normal or nearly so, though it does not fall immediately. In these cases we were particularly cautious about the size of the dose, for a large dose is quite likely to increase the fever, lower the general condition of nutrition, and bring on cachexia. We summarize the total results in febrile cases as follows:

AT TENNOJI.

Temperature.	1st stage.		2d stage.		3d stage.	
	Injections.	Per cent.	Injections.	Per cent.	Injections.	Per cent.
Raised . .	13	17.3	26	14.2	12	9.7
Lowered .	14	18.7	54	29.5	47	37.9
Unchanged .	48	64.0	103	56.3	65	52.4

AT HAMADERA.

Raised . .	21	26.9	66	18.0	27	16.9
Lowered .	11	14.2	55	15.0	60	37.7
Unchanged .	46	58.9	245	67.0	72	75.4

Pulse. No remarkable influence upon the bloodvessels was noted, though in not a few patients the rapidity of the pulse was somewhat reduced and the pulse became somewhat more regular. These phenomena are partly at least, attributable to the fact that the patient is always confined to bed and kept strictly at rest for a certain period.

Perspiration. In the great majority of cases we found the patients somewhat inclined to excessive perspiration. We recognized it in more than 50 per cent. of all patients.

AT TENNOJI.

	Number of patients.	Number of injections.	Number of patients sweated.	Number of injections after which sweating followed.	Percentage as to:	
					Patients.	Injections.
1st stage .	17	75	9	14	53.0	18.5
2d stage . .	36	183	20	36	55.5	19.7
3d stage . .	23	124	13	28	56.5	22.6
	76	382	42	79	55.3	20.6

AT HAMADERA.

1st stage .	21	78	2	3	9.5	3.8
2d stage . .	57	366	21	31	36.8	8.5
3d stage . .	29	109	19	28	65.5	16.5
	107	613	42	62	39.2	10.1

From this table it will be noticed that perspiration after the injection occurred much more frequently at Tennoji than at Hamadera. Especially is the difference noted in cases of the first stage. As our observations were made chiefly in summer, *i. e.*, from May to November, this result could be explained by the difference in temperature due to the respective locations of the two hospitals.³

Perspiration depends somewhat upon the dosage also. The greater the dose the more frequent the sweating. This relation may be clearly seen from the following table:

	Number of patients having frequent sweats.	Percentage.
Above 6.5 c.c.	40	53.2
Under 6.0 c.c.	5	6.5
Under 5.0 c.c.	10	13.0
Under 4.0 c.c.	11	14.3
Under 3.0 c.c.	10	13.0

³ Hamadera is situated on the seashore about ten miles south of Osaka, and is popular as a summer resort because of its relatively cool climate. Tennoji Hospital is situated in the south suburb of Osaka, the greatest industrial city in Japan, and having a notoriously hot climate. The ventilation of the hospital is not ideal.

Perspiration also bears some relation to the number of injections. It is most frequently met with at the first injection and gradually disappears in the course of succeeding injections. This is shown in the following table:

AT TENNOJI.

	1st stage.	2d stage.	3d stage.	Total.	Percentage.
1st injection	7	18	11	36	46.1
2d "	4	6	8	18	23.0
3d "	2	6	4	12	15.4
4th "	1	4	1	6	7.7
5th "	0	1	1	2	2.6
6th "	0	0	1	1	1.3
7th "	0	1	1	2	2.6
8th "	0	0	0	0	0
9th "	0	0	1	1	1.3
10th "	0	0	0	0	0
11th "	0	0	0	0	0
Total	14	36	28	78	100.0

AT HAMADERA.

1st injection	2	13	10	28	40.3
2d "	1	6	8	15	24.3
3d "	0	7	3	10	16.1
4th "	0	1	3	4	6.5
5th "	0	1	2	3	4.8
6th "	0	0	1	1	1.6
7th "	0	1	0	1	1.6
8th "	0	1	0	1	1.6
9th "	0	1	0	1	1.6
10th "	0	0	1	1	1.6
11th "	0	0	0	0	0
Total	3	31	28	62	100.0

In general the perspiration occurs most often in cases of the third stage, but there are many exceptions to this rule.

ACCESSORY EFFECTS. The accessory ill effects of this remedy, which are met with only in rare cases, may be summarized as follows:

(a) Headache and congestion. In a small number of cases (2 to 6 per cent.), headache and congestion were complained of, accompanied by slight fever and flushing of the face. These signs remained only a few days.

(b) Oppressive feelings in the chest are often complained of by nervous and sensitive patients or when excessive dosage is applied. In most cases this symptom vanished within twenty-four hours, and it rarely lasted more than two or three days.

(c) Discomfort in stomach and intestines are felt by those who are suffering from intestinal tuberculosis or from acute or chronic digestive disturbances. This disappears after two or three days. Gastralgia was also noted in some cases.

GENERAL CONDITION AFTER INJECTION. *Subjective.* In many instances no remarkable change in subjective condition is noted. In not a few cases, however, the patient feels quite comfortable and at ease, as if he suddenly became quite free from the illness. This feeling is most common after the first injection, and by the third or fourth injection it is no longer noticed.

Changes in Nutrition. As already repeatedly described all patients are kept at rest for three days after injection, and during this period most of them lost some body weight. The patient was weighed on the day of injection, five days later, and not again until the next injection, two weeks later. We observed that on the fifth day the weight is somewhat reduced in most cases, and only in a small number of cases was it increased. On the day of the next injection, however, the loss is not only quite recovered, but often there is a definite increase in weight. There seems to be a direct relation between body weight and general improvement, *i. e.*, those who gain in body weight are usually much improved while those who lose weight are worse. Loss of weight was almost constant at first when larger doses were used. At that time even those who were strikingly improved lost weight and could not regain it by the time of the next injection. Since the reduction of dosage, however, increase of weight and general improvement run parallel.

We sum up the total results with regard to body weight in the following table:

AT TENNOJI.

	1st stage.	2d stage.	3d stage.	Total.
Weight increased:				
Number of patients	9	18	16	53
Percentage	52.9	77.8	69.6	66.8
Average increase per person . . .	2.006 kg.	2.108 kg.	2.108 kg.	2.130 kg.
Weight decreased:				
Number of patients	8	8	7	23
Percentage	47.1	22.2	30.4	33.2
Average decrease per person . . .	0.363 kg.	1.244 kg.	1.122 kg.	0.9 kg.
Weight constant	0	0	0	0
Maximum increase	5.4 kg.	6.4 kg.	4.35 kg.	
Maximum decrease	0.85 kg.	2.2 kg.	3.3 kg.	

AT HAMADERA.

Weight increased:				
Number of patients	18	44	20	82
Percentage	85.7	77.2	68.9	76.6
Average increase per person . . .	1.811 kg.	2.645 kg.	2.355 kg.	2.391 kg.
Weight decreased:				
Number of patients	2	10	8	20
Percentage	9.5	17.6	27.6	18.7
Average decrease per person . . .	0.9 kg.	1.22 kg.	2.355 kg.	1.643 kg.
Constant (percentage)	4.8	5.2	3.5	4.7
Maximum increase	6.4 kg.	13.2 kg.	5.5 kg.	
Maximum decrease	1.5 kg.	3.0 kg.	4.8 kg.	

It is easy to see from the table how remarkable the results are. It is to be noted that the results are in general better at Hamadera than at Tennoji. We may point out the following factors to explain the difference:

1. The climate in Hamadera is much better than in Tennoji.
2. The equipments are also much better at Hamadera.
3. The patients treated at Hamadera are usually from a class living under better social and economic conditions than those at Tennoji.
4. Patients stay much longer in the Sanatorium at Hamadera than at Tennoji.

We conclude therefore that although the favorable results of the treatment upon nutrition are remarkable, they cannot be attributed to the effect of the remedy alone. The open-air treatment, heliotherapy, hydrotherapy, dietetic treatment, and other routine treatments play an important part in the results.

Next to the increase in body weight, the improvement in the appearance is most remarkable. The anemic or cachectic and exhausted appearance which is so common in patients of advanced stages, with high fever, and especially in those suffering from intestinal tuberculosis, is in most cases wonderfully improved after several injections if the proper dosage has been chosen. The improvement in countenance may come before the restoration of nutrition and the disappearance of fever.

Cough and Expectoration. No remarkable change occurs on the day of injection. On the next day there is an increase of coughing and expectoration in many cases, followed by a gradual decrease. In some cases coughing and expectoration diminish immediately. There are some also in whom no change occurs.

Appetite. In patients suffering from gastro-intestinal disturbances the appetite is more or less affected, sometimes totally lost. This is rare, however, and in a great many cases the appetite remains almost or quite unaffected.

Lung Capacity. To measure the lung capacity we used Hutchinson's spirometer. This apparatus does not always give exact results. No definite conclusions can be drawn, therefore, and we use the measurements only as supplementary material. Results vary widely, showing no definite correspondence with other symptoms, yet in general there seems to be a favorable effect on lung capacity.

Laryngeal Tuberculosis. So far as our limited experience goes the remedy has a stimulating effect in laryngeal tuberculosis, that is, the surrounding parts of the ulcer become hyperemic and reddened for two or three days. Later the redness disappears, the surface becomes granulous in appearance, and the base of the ulcer is somewhat cleansed from caseous masses.

Intestinal Tuberculosis. Further experience is needed before any estimation can be made with regard to the therapeutic value of cyanocuprol for intestinal tuberculosis. As already mentioned the unfavorable reaction can be avoided in a measure if special attention is given to (1) dosage, (2) diet, (3) evacuation of bowel contents. We treated several cases without causing reaction.

Influence upon Tubercle Bacilli. The results of the research vary very widely with respect to the change in number and form of tubercle bacilli in the sputum. We may classify the results as follows:

1. Immediately after the injection the number of bacilli is increased. Later it decreases and in favorable cases the bacilli disappear in a few days.

2. A gradual decrease in number of bacilli takes place without the initial increase.

3. In some cases when the examination of the sputum has been negative it becomes positive after one or two injections, and in the further course of the treatment it becomes again negative or remains positive continuously.

4. The bacilli at first disappear but are found again later.

5. No influence is observed.

We could confirm the facts reported by Koga in some cases, but the time of appearance of such forms as he found does not always bear the same relation to the time of injection. Moreover, such forms may often be seen in the sputa of chronic and cavernous cases. It is impossible, therefore, to decide whether or not such changes are actually caused by this treatment. On the other hand, we saw a patient in whom the sputum had been constantly negative suddenly spit out just after the third injection sputum containing numerous bacilli corresponding to No. X of Gaffky's table. The morphological changes had been noted more often before the reduction of dosage.

Provided the influence be a real one the question whether or not it is the direct effect of the preparation (in the sense of Ehrlich's chemotherapy) still requires investigation.

Hemoptysis. If proper dosage is given the danger of causing hemoptysis is not very great. At Tennoji, among 76 patients and 382 injections, we saw bloody sputum once only in each of 13 patients, and at Hamadera among 107 patients and 613 injections only once in each of 16 patients. The danger is somewhat greater when patients have a history of hemoptysis unless the injections are small and are not given too close to the time of hemoptysis.

At the time when we were still giving large doses, 7 c.c. and 7.5 c.c. were successively given to a patient who had expectorated blood once long before. The symptoms were so much improved that we gave him 8 c.c. at the next injection, attempting to kill all of the bacilli at one blow. On the day after injection, to our great astonish-

ment, the patient raised more than 300 c.c. of blood at one time, the general condition subsequently becoming much worse. The sputum continued bloody for more than a month, so that we were compelled to discontinue the treatment. This case was one of those which led us to the conclusion that the dose should be reduced even if the healing process was thereby retarded. There was a marked decrease in the number of occurrences of this sort after reduction of dosage, with no decided effect upon the efficacy of the drug. Since this bitter experience we have been particularly cautious in cases in which there is any history of hemoptysis. The period of rest is prolonged for such patients and narcotics are prescribed. The intravenous injection of calcium sometimes serves the purpose of a narcotic quite remarkably.

Relation to von Pirquet Reaction. At the spot where the von Pirquet inoculation had previously been made reddening becomes intense, induration increases in degree, and extension after the injection of cyanocuprol. The reaction becomes more intense with each successive injection until after the third to fifth, when the sensitiveness gradually decreases. It is noteworthy that in highly weakened cases, when the reaction ordinarily remains negative, it became positive after several injections.

Indication and Contra-indication. The relatively early cases, those in the first stage, are particularly indicated. Among patients of the second stage the treatment is indicated for those who have a slowly progressing limited lesion. If the affection is widespread or the change quite extensive, it requires great care to select suitable cases for the treatment.

Very much advanced cases, whose general condition is much weakened, or the breathing surface greatly restricted, are contra-indicated. Highly feverish cases, those in which the von Pirquet reaction is negative, or where there has been hemoptysis, are doubtful. Those who have advanced intestinal or laryngeal affections are unfitted for treatment. Patients suspected of general miliary tuberculosis or tuberculous meningitis are certainly contra-indicated. As for cases with recent pleuritis or peritonitis it is better to wait until the first inflammatory process is arrested.

Menstruation is not at all affected. We have no experience with pregnancy.

We very often combined a calcium salt with cyanocuprol to prevent hemoptysis or to prevent the reaction without apparent effect on the healing tendency of the latter. Five to ten c.c. of 5 per cent. solution of calcium chlorid is given intravenously.

Opsonin index is not in most cases increased after the injection.

The content of hemoglobin is increased after several injections.

The number of leukocytes is increased immediately after the injection, but after four to six days decreases again to the original number.

Better results with cyanocuprol are usually obtained in patients previously treated with tuberculotoxoidin.

SUMMARY. 1. Cyanocuprol is very effective in all cases of the first stage. In the majority of cases of the second stage it is also effective. With patients of the third stage it many manifest its effect to a certain extent if favorable cases are selected and proper dosage is given.

2. The effect of cyanocuprol cannot be called strictly chemotherapeutic. It shows in some respects a strong resemblance to tuberculin.

3. The essentials of the treatment with cyanocuprol lie in finding the proper dosage for each patient. If the individualization, which is especially important with this remedy, is properly carried out its value is indeed remarkable, surpassing all other remedies ever tried.

4. The combination of calcium prevents violent reactions and does not affect the efficacy of the drug.

5. The combination of immune therapy and sanatorium treatment is necessary.

6. The question of the duration of the treatment is an important one. According to our own experience if the patient is not improved after two or three injections, or is weakened, the dosage should be reduced or the interval extended. If this brings no improvement the treatment must be given up. Even in favorable cases, when the results are good after each injection, the treatment is best interrupted between the fifth and sixth and eleventh and twelfth injections, for at these times the condition is most improved. If treatment is continued in such cases there will be no benefit from it; instead there may be a return of previous symptoms and the patient's condition may become hopeless.

In conclusion, it is our pleasant duty to pay our best respects to Dr. Koga, and also to express our hearty thanks to Doctors Takagi, Imai, Yukawa, Honda, and Yano for their kind assistance throughout the whole period of our observations.

VAGINAL METASTASES OF HYPERNEPHROMA.

BY GEORGE GELLHORN, M.D., F.A.C.S.,

ASSOCIATE IN GYNECOLOGY, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

THE urinary and genital apparatus in the female are closely connected both topographically and developmentally. In disease this intimate relationship becomes even more apparent. I need but mention the frequent occurrence of pyelitis in pregnancy, the effect upon the bladder of an incarcerated retroflexion of the gravid uterus, the role of cystocele in the etiology of genital prolapse, the relations

of the ureters to cancer of the cervix uteri, the question of vesical fistulae, etc.

The case recorded below is an additional contribution to the borderland between gynecology and urology:

Mrs. Z., aged fifty-four years, referred by Dr. F. R. Fry, complained of severe and persistent pain in the abdomen due to the presence, in the left hypochondrium, of a large, hard and immovable tumor supposed to be retroperitoneal. She had lost thirty pounds in weight within the last few months. Her appetite was poor; the bowels were constipated. There had never been an attack of hematuria or of vesical disturbance.

An irritating and slightly offensive discharge from the vagina, brownish in color and doubly suspicious in a woman past the menopause, called for a vaginal examination. The exploring finger touched two round protuberances springing from the anterior vaginal wall immediately behind the introitus. One of these lay in the median line and the other directly behind it and a little to the right. The elevations were of the size and shape of raspberries, soft in consistency and connected with the vaginal wall by a broad base. Both were easily shelled out with the finger-nail, which procedure left a shallow and but slightly bleeding depression behind. The color of the small growths was grayish red. The rest of the genital system presented no abnormalities; the uterus and ovaries were in a state of physiological atrophy.

The microscopic examination (Dr. G. McConnell*) of the small growths revealed unexpected and highly interesting conditions. In one of them the stroma was made up of a basal layer of connective tissue (Fig. 1). From this sprang a freely anastomosing network of delicate connective-tissue fibers carrying capillaries (Fig. 2). In the peripheral portion such connective-tissue fibers could not be distinguished and the stroma was altogether formed of capillaries which, near the surface, were seen distended with blood. The anastomosing bloodvessels formed distinct alveoli, and these alveoli were densely filled with large polygonal and round cells whose nuclei were well stained. While the contours of the cells were well marked the protoplasm had not taken the stain. In many of the cells there were one or more vacuoles (fat droplets?) while in others a granular arrangement was discernible in the cell body. In some of the cells the nucleus was pushed to one side (Fig. 3). In the periphery of the growth there were several places of hemorrhagic infarct with necrosis of the tissue. In the deeper layers, near the basal connective-tissue wall, there was a reticulum of connective-tissue fibers within which small nests of the same polygonal cells were confined. Deposits of pigment were altogether absent.

* It is a pleasant obligation to thank Dr. McConnell, now in Waterloo, Iowa, for his valuable help.



FIG. 1.—Vaginal metastasis. A freely anastomosing network of delicate connective-tissue fibers forms alveoli which are filled with cells. Note the light color of the alveoli. Bausch & Lomb, 32 mm. Tessar.



FIG. 2.—Alveoli in Fig. 1. enlarged. The connective-tissue septa carry capillaries. Bausch & Lomb, 16 mm. obj. 5 x ocul.

The microscopic picture of the second vaginal growth was somewhat different. The base was made up of a broad band of blood cells without any connective tissue. The contour of the tumor was round, with the exception of one indentation, and was, for the most part, covered with a very thin layer of epithelial cells derived, in all probability, from the mucous membrane of the vagina, and spread out over it like a decidua reflexa (Fig. 4). The stroma was formed by an excessively large number of tortuous and greatly engorged bloodvessels. The endothelial lining of these

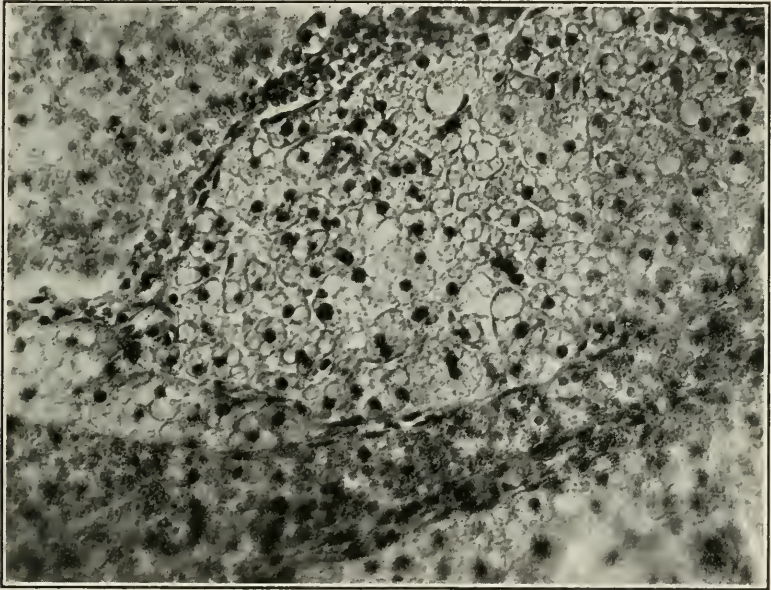


FIG. 3.—In the peripheral portion the alveoli are formed by capillaries. The alveoli are packed with large polygonal and round cells whose nuclei are well stained while the protoplasm has not taken the stain. Many of the cells are arranged in rows and are directly continuous with the endothelium of the bloodvessels without any intervening connective tissue. Note the vacuoles and eccentrically located cell nuclei. Bausch & Lomb, 4 mm. obj. 5 x ocul.

was plainly visible, but other constituents of the vessel walls were absent; connective tissue was discernible in the picture only in faint traces. The parenchyma between the bloodvessels was formed by the same large polygonal cells seen in the other growth. In certain places these cells formed solid columns. Vacuoles and granular arrangement within the cell bodies were also present, but neither pigment nor giant cells could be found. Extravasation of blood had occurred in a few places near the periphery. Round-cell infiltration was observed in two small areas beneath the vaginal covering.

While, thus, in the first picture the alveolar arrangement of the large polygonal cells predominated, the angiomatous condition of the bloodvessels was more conspicuous in the second growth. Both pictures, however, had so many features in common that they had to be considered as various types of one and the same condition.

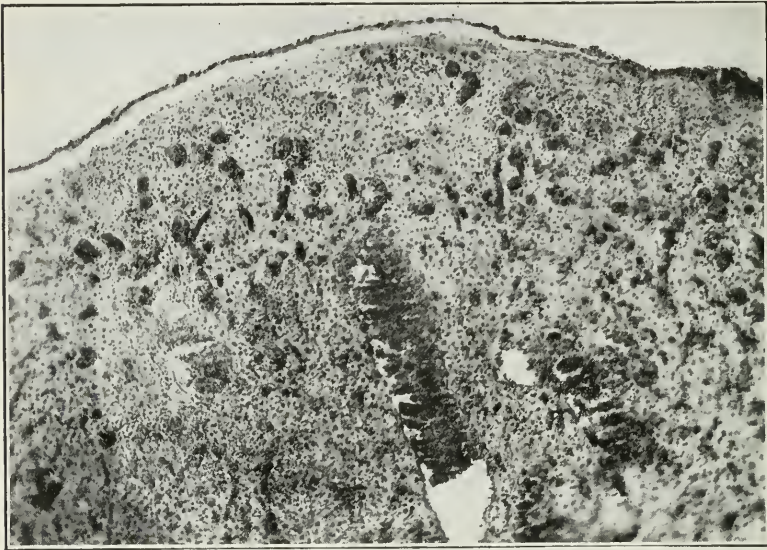


FIG. 4.—Periphery of second vaginal growth. The thin covering is derived from the vaginal mucosa. Note the abundance of tortuous and engorged bloodvessels and the light color of the parenchyma cells. Bausch & Lomb, 8 mm. obj. 5 x ocul.

Both tumors presented microscopically a peculiar glassy appearance, and from the resemblance of their structure to that of the adrenal glands they were interpreted as being hypernephromatous in nature and metastases of the large mass found previously in the left hypochondrium. This latter mass, therefore, was diagnosed as a hypernephroma of the kidney.

That this supposition was correct was proved at the sudden death of the patient three or four days after our diagnosis had been made. At the demand of the family, autopsy was restricted to the abdominal cavity and revealed the hypochondriac tumor to be a typical hypernephroma which had developed from the upper pole of the left kidney. The rest of the abdominal cavity was apparently free from metastases, and from our postmortem findings no definite cause of death could be determined. The two wounds in the vagina resulting from the enucleation of the metastatic growths had almost healed.

The kidney tumor had the size of a large man's fist.* Histologic-

* The tumor was exhibited at the International Surgical Congress in Brussels, but was lost on the way home.

ally, it presented the characteristic features of hypernephroma identical with those found in the vaginal growths. In addition, however, there were also papillary structures in which rows of polygonal cells were arranged along almost invisible capillaries, which in turn branched out from a central bloodvessel of a larger caliber. In several places these rows of cells, two or three deep, had a lumen in the center, caused perhaps by necrosis, thus forming a pseudoglandular arrangement. These gland-like structures were, however, easily distinguished from true glandular spaces which could be observed at about the middle of the microscopic field and were separated from the rest of the tumor by a capsule of connective tissue. We may assume that these glands belonged to the kidney proper and represented urinary tubules.

EPICRISIS. Vaginal metastases of hypernephroma seem to be extremely rare. I have been able to find only the following nine instances of this sort in the literature at my disposal.

1. F. Henke¹ reports the case of a woman, aged sixty years, with multiple tumors of the vagina, which, at first, were thought to be metastases of uterine cancer. Besides, she had a pedunculated tumor of the skin of about the size of a goose egg and the shape of a mushroom. Postmortem revealed the presence of a typical malignant hypernephroma of the left kidney. This latter tumor as well as the growths in the skin and vagina contained a large amount of glycogen and presented identically the same microscopic picture. The cutaneous and vaginal tumors must therefore be considered as metastases of the suprarenal tumor.

2. A. von Rosthorn² demonstrated a vaginal metastasis of an "hemendothelioma" of the kidney. I was unable to find the original report. The name hemendothelioma, however, suggests that von Rosthorn presented his case at a time when the histogenesis of these tumors was still under discussion. Driessen,³ Hildenbrand⁴ and others believed that they originated from the endothelium of bloodvessels and lymphatics. As we shall see later the term "hypernephroma" has now been generally accepted, and Kelly⁵ expressly states that this term includes the "endothelioma" of Driessen as well as the "angiosarcoma" of De Paoli, Beneke and Sudeck.

The case of von Rosthorn, however, is rather doubtful. Schottlaender³⁰ quite recently classified this case among those of "ectopic chorio-epithelioma."

3. Peham⁶ speaks of a woman, aged fifty-nine years, who, for a few months, had complained of a bloody vaginal discharge; one and one-half years previously she had some urinary discomfort, and once there was an attack of hematuria. On examination a large hypernephroma of the left kidney was found. The anterior vaginal wall was infiltrated and a sessile growth the size of a hazelnut was discovered directly behind the introitus. The structure of this growth, on microscopic examination, was identical with that of the hypernephroma.

4. R. Freund⁷ reports a vaginal metastasis in a woman, aged fifty-six years, which had appeared one and one-half years after the extirpation of the left kidney for "sarcoma." The metastatic growth had the size of a cherry; it was located upon the anterior vaginal wall to the left of the urethra, and had caused hemorrhages for the past six months. The microscopic examination of both the primary and metastatic tumors revealed typical hypernephroma.

5. Hoffmann⁸ found in a woman, aged sixty-one years, a cauliflower growth in the vagina as a metastasis of a hypernephroma of the left kidney. There were numerous other metastases throughout the body.

6. Alban Doran⁹ described in detail the findings in a woman, aged forty years, whose right kidney was extirpated for hypernephroma. Aside from metastases in the liver and lungs, there were several metastatic growths, both sessile and pedunculated, within the vagina.

7. In the discussion following Doran's paper, Overy³⁴ described a similar case in which a polypoid mass had been found attached to the anterior vaginal wall. This was removed and a large tumor in the right side of the abdomen was discovered. Two months later the vaginal growth had recurred and it was again removed. The patient died a month later. The postmortem examination showed that the abdominal tumor was primary and was a malignant adrenal tumor starting in an adrenal rest. There were numerous secondary deposits in the liver and lungs, sections of which showed more or less typical adrenal tissue.

8. Graefenberg¹⁰ found, in a woman, aged fifty-four years, a tumor of the left kidney and two nodes of walnut and hazelnut size respectively upon the anterior and posterior vaginal walls immediately behind the introitus. Microscopic examination of these nodes revealed the picture of malignant hypernephroma. The vaginal growths obviously were metastases of the renal tumor.

9. Graefenberg¹⁰ discovered, in a woman, aged sixty-five years, a deeply pigmented tumor of the vulva in the vicinity of the meatus urinarius. Microscopically the tumor showed the characteristics of hypernephroma, and upon autopsy, a malignant hypernephroma of the left kidney the size of a child's head was found. The growth in the vulva was the only metastasis of the renal tumor.

An interesting feature of my own case is the fact that the microscopic examination of the vaginal metastases enabled us to correctly diagnose the primary tumor. In like manner did Graefenberg¹⁰ diagnose both his cases of hypernephroma from a histological examination of the secondary manifestations. Indeed, it is often only the metastasis which causes the patient to seek medical aid while the primary tumor, for the time being, produces no symptoms at all. Thus Hoffmann¹¹ found in a man who entered the hospital, because of pain in his leg, a metastasis in the femur which led him to

search for and find a hypernephroma of the kidney; and Israel¹² and Albrecht¹³ likewise observed bone tumors which, after careful observation, were recognized as metastases of a hitherto obscure hypernephroma.

In my case the vaginal tumors, which from their proximity, may be considered as one, were clinically the only metastasis in the body; but as the autopsy had to be limited to the abdominal cavity the possibility of other metastases in the brain or thoracic cavity cannot definitely be excluded. Contrary to the opinion of Berg³¹ there are but very few instances of solitary metastases of hypernephroma in literature. The case of Graefenberg¹⁰ has already been referred to. In one of Albrecht's cases¹³ a metastasis in the scapula was the only one in the body.

As a rule, however, hypernephroma causes multiple metastases. They are most frequently found in the bones and lungs, but since the disease is disseminated by way of the bloodvessels, almost all organs may become affected. Hoffmann⁸ describes hypernephroma metastases in brain, liver, lungs, kidney, bronchial glands, various bones, the skin of the thigh and the vagina. Funccius¹⁴ reports metastases in the ovary and pancreas, and Garceau¹⁵ mentions, in addition, metastases in spleen, uterus, intestines, bladder and omentum. Harttung³³ recently recorded a metastasis in the spine.

In view of this multiplicity of metastasation in the various parts of the body the rarity of vaginal metastases is doubly remarkable. Graefenberg¹⁰ endeavors to explain this phenomenon. He says that particles of the tumor usually enter the vena cava through the renal vein; thence they are carried through the heart into the pulmonary arteries. This, however, explains merely the frequency of metastasis in the lungs. According to Sutter's investigations, retrograde metastases of malignant kidney tumors may at times be disseminated throughout the entire genito-urinary apparatus by way of the vena spermatica. This possibility seems plausible in cases in which metastases are found in the ovaries, uterus and upper portions of the vagina for these localities are exposed to retrograde transportation of tumor particles by way of the spermatic vein through anastomoses with the plexus pampiniformis. This explanation, says Graefenberg, is, however, not sufficient for metastases in the lower portion of the vagina and the vulva. Tumor particles from the kidney can reach the vulva by way of the spermatic vein only if there is an anastomosis of the plexus pampiniformis with the obturator vein. Such an anastomosis exists at times. The obturator vein, again, receives rami pubici from the external genitals, and thus a direct communication from the renal vein to the vulva is established. Since the left spermatic vein empties into the left renal vein, such a retrograde transportation of tumor particles to the external genitals seems more likely on this side than on the other because, under ordinary circumstances, the right spermatic vein does not empty into the renal vein but directly into the vena cava.

Graefenberg's contentions are borne out by the studies of Kownatzki¹⁶ on the distribution of veins in the female pelvis. Kownatzki depicts in Fig. 4 an old parametritis which has led to an anastomosis between the plexus pampiniformis and the obturator vein. He furthermore shows in his dissections that even without such an anomaly the pubic veins carry blood from the external genitals directly into the so-called median iliac vein which by means of the uterine veins is connected with the spermatic vein and thus with the renal vein.

The theoretical explanation of Graefenberg is supported by the fact that of the 10 hypernephromata here collected, 7 were on the left side. In 1 case the location of the tumor was not stated. In the case of Doran the hypernephroma was situated on the right side; the metastases were in the upper portion of the vagina and therefore do not come within the scope of this particular consideration. In Overy's case the exact location of the metastasis is not given. The preponderance of hypernephroma on the left side in these cases does not seem accidental. Keyes¹⁷ says that renal growths are about equally frequent on the two sides, and Garceau¹⁵ states: "The right side is a little more frequently affected than the left; 82 cases are recorded in which the disease occurred on the right, 77 on the left and in 17 the side was not stated." In contradistinction to these statistics, among which there are a number of individual observations, I find that the proportion is reversed if we consider whole series of cases reported by one and the same author, as in the following table:

Author.	Right.	Left.	Not stated.	Total.
Israel ¹²	7	10	0	17
Kelly ⁵	1	4	1	6
Albrecht ¹³	9	19	0	28
Scudder ¹⁸	2	3	1	6
	19	36	2	57

The diagnosis of hypernephromatous metastases in the vagina rests upon the microscopic examination. These metastases reproduce exactly in their minute structure the characteristics of the parent tumor (Garceau), and the latter, again, suggests histologically the structure of the cortex of the adrenal. It will be remembered that the adrenal gland is composed of a medullary and a cortical portion. The latter is subdivided into three more or less distinct layers, the *zona glomerulosa*, *zona fasciculata* and *zona reticularis*. In the case of tumor formation, however, these three layers are not evenly represented; the fascicular layer usually predominates. Moreover, as the tumor grows, atypical formation can occur, which may resemble adenoma, sarcoma, endothelioma, or carcinoma.³² This variability of the microscopic picture has been the cause of much confusion until Lubarsch¹⁹ and Birch-Hirschfeld²⁰ suggested

that an indifferent name should be chosen which would leave the question of histogenesis in abeyance and would merely signify that these tumors were derived from the adrenal. The name "hypernephroma" proposed by them has now been almost generally accepted.

That these tumors were of adrenal origin was first shown by Grawitz²¹ in 1883, who, moreover, proved that the tumor formation did not so much take place in the adrenal proper as in "aberrant" adrenal tissue, which is so frequently found in the kidney. Such aberrant adrenal tissue was later demonstrated in all parts of the abdomen, but particularly in the urogenital tract, by Imbert, Schmorl,²² Marchand, Chiari, Hanau, Ulrich, Targett,²³ Aichel,²⁴ Pick,²⁵ and numerous others. Consequently, primary hypernephromata originating from these so-called adrenal rests have been observed in organs other than the kidneys. Thus, Keen, Pfahler and Ellis,²⁶ in a collection of 163 cases, found 157 in the kidney, 3 in the adrenal, 2 in the liver and 1 in the uterus. Pick²⁴ and Bovin²⁷ described primary hypernephroma in the ovary and Weiss²⁸ a like tumor in the broad ligament.

Although usually of slow growth, hypernephroma is potentially a malignant tumor, and metastasation will occur sooner or later. These metastases are almost always multiple, as mentioned above, and their presence contra-indicates any operation.

To return now to vaginal metastases with which we are here more particularly concerned, they are of considerable practical importance to the gynecologist. As Freund⁷ justly points out, metrorrhagias or a bloody vaginal discharge, after a previous nephrectomy, should make us think of metastases of hypernephroma, particularly if the anterior vaginal wall near the introitus is affected.

Malignant tumors of the vagina are usually considered primary. It seems but reasonable to think that in some such cases the tumor is in reality a metastasis (Veit²⁹). If more attention would be given to this point in future the bad prognosis of malignant new growth of the vagina would, to a certain extent at least, be explained. It is not at all illogical to surmise that many a supposed sarcoma or carcinoma of the vagina will, on careful microscopic examination, prove to be hypernephromatous in nature and that a thorough investigation will lead to the discovery of the tumor in the kidney.

SUMMARY. In a woman, aged fifty-four years, a large retroperitoneal tumor on the left side was found whose nature could not be determined. Vaginal examination revealed the presence of two growths in the anterior vaginal wall near the introitus. These growths were of the size and shape of raspberries and were easily shelled out with the finger-nail. Microscopic examination showed typical hypernephroma. It was then assumed that the two vaginal growths were metastases of the obscure retroperitoneal tumor and that the latter was a hypernephroma of the kidney. The patient

died suddenly a few days later and autopsy fully confirmed the correctness of the diagnosis.

Vaginal metastases of hypernephroma are extremely rare. Literature contains but 9 other instances of this kind. It is, however, probable that many cases of primary sarcoma of the vagina are in reality hypernephromatous in nature and secondary to a malignant tumor of the kidney.

BIBLIOGRAPHY.

1. Henke: Tr. German Pathological Society, 1906, p. 261.
2. Rosthorn, A. von.: Quoted from Henke¹.
3. Driessen: Ziegler's Beitr. z. path. Anat., 1892, xii, 65.
4. Hildenbrand: Langenbeck's Arch. f. klin. Chir., 1894, xlvii, 225.
5. Kelly: Ziegler's Beitr. z. path. Anat., 1898, xxiii, 280.
6. Peham: Zentralbl. f. Gynäk., 1906, xxx, 724.
7. Freund, R.: Zentralbl. f. Gynäk., 1908, xxxii, 304.
8. Hoffmann: Zentralbl. f. Chir., 1907, xxxiv, 82.
9. Doran, Alban: Jour. Obst. and Gynec. of British Empire, 1907, xi, 448.
10. Graefenberg: Virchows Arch. f. path. Anat., 1908, exciv, 17.
11. Hoffmann: Deutsch. med. Wehnschr., 1907, xxxiii, 303.
12. Israel: Chirurg. Klinik der Nierenkrankheiten, Berlin, 1901.
13. Albrecht: Arch. f. klin. Chir., 1905, lxxvii, 1073.
14. Funceius: Inaug. Diss., Erlangen, 1905, quoted from Graefenberg¹⁰.
15. Garceau: Tumors of the Kidney, New York and London, 1909.
16. Kownatzki: Die Venen des Weiblichen Beckens, Wiesbaden, 1907.
17. Keyes: Diseases of the Genito-urinary Organs, New York and London, 1911.
18. Scudder: Ann. Surg., 1906, xlv, 8.
19. Lubarsch: Virchows Arch. f. path. Anat., 1894, cxxxv, 195.
20. Birch-Hirschfeld: Lehrb. d. path. Anat., 1896, 5th edition, i, 262.
21. Grawitz: Virchows Arch. f. path. Anat., 1883, xciii, 58.
22. Quoted from Garceau¹⁵.
23. Borst: Die Lehre von den Geschwuelsten, Wiesbaden, 1902, p. 790.
24. Aichel: Arch. f. mikroskop. Anat., etc., 1900, vol. lvi.
25. Pick: Arch. f. Gynäk, 1901, vol. lxiv.
26. Quoted from Garceau¹⁵.
27. Bovin: Surg., Gynec. and Obst., 1910, x, 109, abstr.
28. Weiss: Quoted from Borst²³.
29. Veit: Discussion of Freund's paper⁷.
30. Schottlaender: In H. Nothnagel's spezielle Pathologie und Therapie, Supplement, 1913, No. 7; ii, 515.
31. Berg: Surg., Gynec. and Obst., October, 1913, No. 4, xvii, 463.
32. Adami: Principles of Pathology, 1909, ii, 768.
33. Hartung: Deutsche. med. Wehnschr., 1914, xl, 1249.
34. Overy: Jour. Obst. and Gynec. of British Empire, 1907, xl, 510.

WAR MEDICINE

CONTRIBUTORS.

- LIEUTENANT-COLONEL SIMON FLEXNER, M.R.C., U. S. A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U. S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- COLONEL FREDERICK F. RUSSELL, M.C., U. S. A.
- DR. RICHARD M. PEARCE, National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, U. S. N. A.
- MAJOR R. M. YERKES, Sanitary Corps, U. S. A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- DR. E. E. SOUTHARD, Director of Psychopathic Department, Boston State Hospital.
- LIEUTENANT-COLONEL WARFIELD T. LONGCOPE, U. S. N. A. (Prof. Practice of Medicine, Columbia University).
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- DR. A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- LIEUTENANT O. H. PERRY PEPPER, M.R.C., U. S. A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Prof. of Pediatrics, Univ. of California).
- MAJOR FRED H. ALBEE, M.R.C., Director of Military Reconstruction Hospital No. 3, U. S. A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.R.C., U. S. A.
- DR. JOHN A. HARTWELL, Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- CAPTAIN RALPH PEMBERTON, M.R.C., U. S. A.
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

A REPORT OF THIRTY CASES OF MENINGOCOCCIC CEREBROSPINAL MENINGITIS.

BY GUTHRIE McCONNELL,
MAJOR, M. R. C.,

MYRON L. MORRIS,
MAJOR, M. R. C.,

AND

NEWTON A. SEEHORN,
CAPTAIN, M. R. C.

(From the Laboratory of the Base Hospital, Camp Pike, Arkansas.)

BELIEVING that a discussion of the clinical aspects of cerebrospinal meningitis might be of some value, we report a series of 30 cases that have been admitted and treated in the Base Hospital, Camp Pike, Arkansas, during November and December, 1917.

In the majority of instances the cases have been admitted within twelve to forty-eight hours after the appearance of symptoms, but a few were practically moribund at that time and died within a comparatively few hours. These, however, are included in the report.

For various reasons the meningitis patients have been turned over to the laboratory department, not only as regards diagnosis, but also treatment, a ward in the hospital being set aside for that purpose. The greatest part of the work has been done by Captain Morris and a much smaller amount by Captain Seehorn and Major McConnell.

SYMPTOMS ON ADMISSION. Although several of the patients were unconscious on admission, it was possible, as a rule, to elicit definite information concerning the subjective symptoms. In order of frequency they were as follows: (1) profound frontal headache; (2) stupor or coma; (3) rigidity of the neck; (4) vomiting; (5) Kernig's sign; (6) increased knee-jerks; (7) hyperesthesia; (8) slow pulse; (9) petechiæ; (10) slight increase in temperature. Strabismus was not present as an early symptom.

Headache. The headache was very severe in character, being much more marked than in typhoid fever, and nearly always was frontal. In one case in which it became basilar the patient lapsed into coma and finally died.

Mental Condition. In regard to the mental condition, there were all variations from an almost abnormal acuteness to complete coma. As a rule the patient was dull and inclined to sleep, but could be aroused, at which times he would appear irritable. Otherwise he would remain quiet, and breathing would be of a normal type, quite unlike that of the alcoholic, uremic or apoplectic.

Rigidity of the neck was, as a rule, well marked and accompanied by more or less retraction. In some instances this reached the point of a mild degree of opisthotonos. Any attempt at flexion, either active or passive, was painful, and evidently this rigidity was in no way due to the will of the patient. In this respect it differs from that seen in poliomyelitis, as in the latter the patient voluntarily resists, knowing that any motion will be painful. If this stiffness is not noticeable early it soon becomes very evident.

Vomiting occurred in about two-thirds of the cases and was of the projectile or cerebral type, coming without warning and without previous nausea. In a few of the cases it was the initial symptom.

Kernig's sign was positive in nearly every case, either slight or well marked, according to the general condition of the patient; but as it is found in various other infections, it is not of great diagnostic value. It was noted, however, that just at the moment when knee extension was made, after full flexion of the hip, both pupils dilate promptly and markedly. This same phenomenon was noted when flexion of the neck was attempted.

The knee-jerks were exaggerated in most of the cases, as were the plantar reflexes. Babinski's sign was absent in practically every case.

Hyperesthesia was present in many instances to a high degree and at times the skin showed marked irritability, as evidenced by positive "tâche cérébrale."

The pulse in nearly every case was slow, commonly between sixty and seventy, and not unusually it was in the fifties; as a rule a full volume, but occasionally irregular or intermittent, or both. The rate seemed to have little relation to the degree of temperature.

Petechiæ were present in but a small percentage of the cases, being marked in but three. Generally the distribution was diffuse, with variations in size and shape and not disappearing on pressure. In those showing well-marked petechiæ the other symptoms were severe, including a markedly purulent cerebrospinal fluid occurring in large amount, with a great increase in globulin.

Temperature. The temperature has not been high, particularly early in the disease. On admission the temperature was, as a rule, less than 101° , and even some of the worst cases did not go over 100.5° . The highest that was noted was 104.5° , except in one case in which it went up to 107° shortly before death. As compared with the English report the average temperature at the time of admission in our series was distinctly lower.

Various other symptoms were noted but did not appear with sufficient regularity to make them of diagnostic importance.

Strabismus of the convergent type was rather frequent.

Deafness was usually mild, but at times was well marked, was quite common, and generally persisted for a longer time than did the strabismus.

Herpes appeared in practically all of the cases and were abundant, usually most extensive on the lips at the mucocutaneous junction. The ears, nose and forehead were involved also. In several patients the herpes were so extreme that a good part of the face was covered by large scabs and the nose or an ear was swollen to twice its normal size.

The procedure in the cases was as follows: When the patient was admitted to the hospital he was seen by the medical officer, and if meningitis were suspected the laboratory was notified. A physical examination was made, and if it were decided to make a lumbar puncture the patient was sent to the meningitis ward. The skin over the junction of the fourth and fifth or third and fourth lumbar vertebræ was painted with iodine and a puncture made. If the patient were unconscious no anesthetic was used, as a rule. If slightly conscious and restless a mild chloroform anesthesia was employed. If fully conscious the patient was told what was to be done and no anesthetic was given. As a rule, general anesthesia was not used, as there seemed to be very little difficulty in removing considerable quantities of fluid, in one case as much as 125 c.c. On removing the stylet from the needle the first part of the fluid was allowed to flow into a sterile test-tube, then a small amount into a tube of culture media (serum dextrose agar). If the fluid were turbid the canal was allowed to drain and a dose of antimeningitis serum injected at once, the diagnosis being made later. It has happened in three instances that the cause of the condition was found to be the pneumococcus. These are not included in this series. Irrespective of the total amount of fluid removed, provided that it was more than 45 c.c., there was injected immediately 40 c.c. of serum. Whenever the quantity obtained was less than 45 c.c. the rule of injecting an amount of serum 5 c.c. less than that of the fluid withdrawn was followed.

If the spinal fluid were clear a globulin test and a cell count was made.

If either or both of these indicated a spinal irritation a dose of serum was given.

In regard to the pressure under which the fluid flowed it was observed that practically all the cases showed an increase, either moderate or marked. Inasmuch as an increased pressure was found in a number of cases that proved to be negative, this condition was disregarded as a positive indication for the injection of serum. Reliance was placed upon the character of the fluid, the presence of globulin and the cell count. The spinal fluid was centrifuged and the diagnosis confirmed by finding an abundance of polymorphonuclear leukocytes and a Gram-negative diplococcus. A positive diagnosis was made from the cultures on the basis of the appearance of the colonies and the finding of Gram-negative diplococci. Agglutination was not resorted to to determine the type of the organism on account of lack of personnel and of material. The fact that the cases with but very few exceptions showed improvement following the first injection of the antimeningitis serum would seem to indicate the correctness of the diagnosis.

In the examination of the sediment obtained by centrifuging the cerebrospinal fluid the organisms show the general morphology of the meningococcus. There was, at times, considerable variation in the size, shape and position in regard to the polymorphonuclear leukocytes. Most of the cocci were large "biscuit" shaped, arranged in pairs, as a rule, but sometimes like tetrads. Others were smaller and more rounded. They were found both extra- and intracellularly, as has been reported by many investigators. Consequently not much weight was attached to location. Many appeared to be within the nuclei of the leukocytes. The organisms were uniformly Gram-negative. The number present varied greatly, some cases containing thousands, while in others, apparently of equal severity, it was with the greatest difficulty that any could be demonstrated. It was noted, as has been reported by the English Commission, that after the first injection the organisms were greatly diminished in those cases in which they had been numerous, and that after the second or third injection they could not be demonstrated.

In the more severe cases, when the fluid was allowed to stand for a short time, a diffuse gelatinous coagulum formed, this eventually settling to the bottom of the test-tube. The coagulum was very tenacious and could not be removed piecemeal. The uncoagulated part of the fluid remained cloudy, and on being centrifuged, pus cells and meningococci could be demonstrated.

ADMINISTRATION OF SERUM. In giving the serum the gravity method was not employed. Instead a Luer syringe of 40 c.c. capacity was used, there being a rubber tube with nipples for connection with the syringe and the needle. The serum was injected very slowly, but in many instances gave rise to more or less severe cramp-like pains in the lower extremities; these, however, were only temporary and did not require any treatment. It was very seldom that any untoward symptoms developed, the respirations continued without interruption and the pulse did not become rapid or weak. No attempts were made to follow Sophian's scheme of taking the blood-pressure at the time of injection.

In giving subsequent treatments the same methods were used and as

much fluid as would readily flow was removed. The amount obtained varied greatly, the maximum amount being 150 c.c. and the minimum 5 c.c. Both these cases resulted fatally.

AMOUNT OF SERUM GIVEN AND FREQUENCY OF INJECTIONS. All of the cases, as soon as the lumbar puncture was done, and either a cloudy fluid discovered or a positive globulin obtained, were given, as a rule, 40 c.c. of serum. As already stated, the dose depending upon the amount of fluid withdrawn, in most instances the initial puncture yielded upward of 50 c.c. According to our experience it would appear unnecessary to give the serum more frequently than at twenty-four-hour intervals excepting in those fulminating forms when death seems imminent. One patient received four injections within thirty-six hours and showed improvement after each treatment. With but two or three exceptions the first three injections were given at twenty-four-hour intervals. The period between treatments was increased only when the temperature had been down to normal for at least thirty-six hours and when the last puncture had yielded a fluid decidedly less turbid than that obtained at the initial puncture. The globulin reaction (Noguchi method) also was used as a guide as to the time interval and prognosis. As the fluid became less turbid the globulin diminished relatively. Thus from a four-plus reaction at the first it would diminish, as a rule, so that by the third lumbar puncture the reaction would be one plus or less. Consequently, when the fluid decreased in turbidity, regardless of the amount obtained when the temperature had been normal for a minimum of thirty-six hours and when the globulin reaction came down to one plus or less, it seemed safe to wait forty-eight hours or perhaps longer before another injection was given. This depended, of course, as to whether or not any disturbing symptoms made their appearance.

Regarding the globulin reaction it was noted that the patient occasionally showed a marked improvement, yet the globulin did not go below two plus. At such times it is safe to disregard the globulin and wait forty-eight hours before treating. The persistence of the reaction may be due to the irritation of the serum or to the puncture itself.

Many of the cases will need no further serum after the fourth dose, yet it may be well to make a puncture at the end of forty-eight or seventy-two hours later to determine the pressure, the quality and quantity of the fluid and the globulin reaction. It might be recommended that in spite of the above findings being negative the patient be given another dose. In this connection it was observed that if after an interval of forty-eight or seventy-two hours another dose is given to a case that shows apparent recovery a violent reaction may occur. This reaction is far more severe than that following any previous injection. The temperature rises abruptly, the pulse increases markedly in rapidity and is occasionally irregular, pain in the back becomes acute and even a wild delirium has occurred. These symptoms subsided in from twelve to eighteen hours without any unpleasant sequelæ. In spite of the possibility of such a reaction it has been deemed advisable to give the additional injection.

If the patient does not show improvement it may be necessary to continue the lumbar punctures until recovery or death ensues. In one case, which finally proved fatal, twenty-three lumbar punctures were made.

The daily course of the disease showed interesting changes. Many of the patients were admitted, in a semicomatose condition that made it impossible to get any very clear statements. For that reason it was generally an easy matter to determine the effect of the serum by noting whether there was or was not any decrease in the stupor. Practically all of these cases showed signs of returning consciousness within six hours after the first injection. Within twelve hours nearly all could tell clearly events which took place up to the time of becoming unconscious, occasionally remembering some trivial occurrence during the period of coma. This happened even in four of the fatal cases.

The following signs of improvement were considered of value in the order given, and on them was based the prognosis of the case: (1) improvement in the consciousness of the patient; (2) fall in temperature to nearly normal; (3) diminution in intensity of headache; (4) no decrease or marked increase in the pulse rate; (5) no increase in the rigidity of the neck; (6) decrease in the globulin. It would seem that the early signs of improvement, those appearing within six hours after the first injection of the serum, are due, in part, to the fall of intracranial pressure, following the withdrawal of the large amount of cerebrospinal fluid. For this reason it does not seem advisable to base a favorable prognosis on very early improvement. If, however, the above-mentioned signs are still present at the end of twenty-four hours the probabilities are that the disease is yielding to the treatment. It must be remembered though that this form of cerebrospinal meningitis is a very capricious disease and must be watched carefully. If these indications of betterment were still present after twenty-four hours the improvement continued almost miraculously and with progressive rapidity. The favorable cases, by the end of thirty-six hours, became entirely conscious and were interested in what was being done for them. After this stage the temperature rarely rose above 101° and in most instances went no higher than 100° . All temperatures were rectal. The headache disappeared but the patients still had very vivid recollections of its terrific intensity. The pulse rate was usually about the same as on admission, or very slightly increased, generally of good quality and regular. Some of the cases, however, on admission had intermittent and irregular pulses. By this time the stiffness of the neck was less marked and the excruciating pain formerly present when attempts at flexion were made was absent. Some of the patients, even at this early stage, had complete lateral motion, with a fair degree of flexion.

As the favorable course continued it was within three to five days that most of the cases felt practically normal, except for a feeling of weakness, of which they all complained. This was most marked in the back and neck, probably due to the fact that the muscles of these regions had been contracted spasmodically for so long that more or less of the muscular tonicity had been lost.

The well-known observation that in practically all fevers an ascending pulse with a descending temperature is of bad prognostic import was emphasized in this series of meningitis. This was demonstrated very clearly in one of the fatal cases. He at first seemed to be doing as well as the others, yet his pulse rate increased progressively while his temperature decreased. He received twenty-three intraspinal inoculations of serum. This case terminated fatally.

No.	Initials.	Stage when treatment was begun. Approximate.	Number of lumbar-punctures.	Amount of serum given.	Complications.	Period to convalescence or death.
1	J. O.	24 hours	7	205 c.c.	None	Oct. 31 to Nov. 7; cured.
2	J. F.	24 hours	11	320 c.c.	None	Nov. 8 to Nov. 18; cured.
3	J. V.	At least 18 hours	23	695 c.c.	None	Nov. 9 to Dec. 6; died.
4	F. F.	Admitted Oct. 29 Treated Nov. 11	16	440 c.c.	Broncho-pneumonia	27 days; died.
5	J. B.	24 hours	6	150 c.c.	None	Nov. 11 to Nov. 16; cured.
6	A. McM.	24 hours	23	555 c.c.	None	Nov. 11 to Dec. 8; cured.
7	H. D.	36 hours	5	125 c.c.	None	Nov. 12 to Nov. 15; cured.
8	F. J.	24 hours	6	155 c.c.	Orchitis	Nov. 13 to Nov. 20; cured.
9	G. M.	36 hours	7	110 c.c.	None	Nov. 15 to Nov. 29; cured.
10	F. S.	40 hours	10	210 c.c.	Orchitis	Nov. 16 to Dec. 11; cured.
11	L. D.	At least 24 hours	17	440 c.c.	Esophageal spasm	19 days; died.
12	M. H.	48 hours	15	345 c.c.	Esophageal spasm	Nov. 20 to Dec. 4; cured.
13	P. W.	24 hours	4	120 c.c.	None	Nov. 20 to Nov. 23; cured.
14	O. D.	48 hours	11	345 c.c.	None	Nov. 24 to Dec. 4; cured.
15	W. R.	5 days	1	40 c.c.	None	6 days; died.
16	J. T.	72 hours	5	120 c.c.	None	Dec. 3 to Dec. 8; cured.
17	G. S.	Over a week; low grade	4	105 c.c.	None	Dec. 2 to Dec. 8; cured.
18	A. W.	36 hours	8	200 c.c.	None	Dec. 4 to Dec. 12; cured.
19	C. M.	24 hours	4	110 c.c.	None	Dec. 7 to Dec. 10; cured.
20	J. H.	36 hours	5	120 c.c.	None	Dec. 9 to Dec. 16; cured.
21	W. B.	72 hours	4	140 c.c.	None	Dec. 14 to Dec. 17; cured.
22	R. P.	48 hours	1	40 c.c.	Anaphylaxis	Few hours; died.
23	R. W.	48 hours	5	135 c.c.	None	Dec. 16 to Dec. 20; cured.
24	M. J.	24 hours	5	110 c.c.	None	Dec. 18 to Dec. 22; cured.
25	J. S.	24 hours	3	90 c.c.	None	Dec. 20 to Dec. 22; cured.
26	W. C.	24 hours	3	75 c.c.	None	Dec. 20 to Dec. 22; cured.
27	W. R.	48 hours	2	40 c.c.	None	Dec. 23 to Dec. 25; died.
28	H. G.	24 hours	14	340 c.c.	None	Dec. 25 to Jan. 9; died.
29	C. H.	24 hours	5	140 c.c.	None	Dec. 25 to Jan. 1; cured.
30	A. W.	24 hours	4	120 c.c.	None	Dec. 29 to Jan. 1; cured.

Complications. There were but two complications that made their appearance, orchitis and esophageal spasm. Orchitis occurred in two instances, one being unilateral and the other bilateral. The testicle involved was enlarged, and was extremely painful and tender. The epididymis, however, was not attacked. The process subsided under rest and the application of ice-caps. A venereal history was denied by both patients, and in neither were there any indications of any past or present trouble. In addition the absence of involvement of the epididymis would seem to favor the non-venereal character of the orchitis.

The other complication also appeared in 2 of the cases, both of which complained of difficulty in swallowing even liquids. In one of them the spasm cleared up very shortly without any special treatment. In the other the spasm persisted and attempts to feed by means of the stomach-tube were made. The first feeding was successful, but after that it became impossible to pass the tube into the stomach even under chloroform anesthesia. The tube would traverse about three inches of the esophagus, beyond which point it would not pass and would begin to coil upon itself. After several attempts were made a gastrostomy was performed. Twelve hours later the patient died, more from asthenia due to lack of nourishment than from the result of the operation or from marked pathological changes, due to the meningitis. Rectal feeding had been tried, but nothing was retained.

In addition to the above-mentioned complications certain other conditions developed in the course of the disease. The most common were serum sickness and urticaria. Most of the cases developed an urticaria in from seven to ten days after the first serum injection. In seeking for a cause for this late occurrence the conclusion was reached that the repeated intraspinal injections of serum gradually increase the permeability of the choroid plexus so as to allow the passage of the serum into the blood stream. That this process takes place on an extensive scale is evidenced by the fact that the urticaria produced is widespread and abundant. In this respect the action is interesting when compared with that of the intravenous injections of salvarsan, as with that there is very little, if any, passage of arsenic into the cerebrospinal fluid. Some of the herpes developed upon the urticarial wheals and thus produced a peculiar eruption.

So was stated in the British report, and as has been our experience, no symptoms of acute anaphylaxis have developed; the urticaria has been the only indication of active serum sickness. In one instance there was a very unfortunate occurrence. This patient was admitted in a moribund condition with his body covered by a diffuse petechial rash. He was given 40 c.c. of antimeningococcus serum immediately upon the removal of the spinal fluid. Three hours later it was decided, on account of the evident severity of the case, to give some serum intravenously. Forty cubic centimeters were given and within a few minutes after the withdrawal of the needle an acute superficial edema appeared, most noticeable in the eyelids, which rapidly became swollen, and within fifteen minutes the patient died from respiratory failure. At the time that it was decided to give the intravenous injection the question of anaphylaxis was considered, but in view of the fact that 40 c.c. of serum had been given intraspinaly three hours before, without any disturbances occurring, it was decided to give the serum intravenously. This result substantiates the belief that it is not until repeated injections have been given that the choroid plexus becomes permeable.

So far as the autopsy reports are concerned there was comparatively little found; the findings were as follows:

CASE I.—J. J. V. Purulent meningitis, chiefly basilar, but some slight general involvement. Lateral ventricles contained an increased amount of fluid, quite turbid in appearance. Large amount of cerebrospinal fluid. Scattered areas of bronchopneumonia of right lower lobe, with slight purulent pleuritis. Pneumococci found in smear from pleura.

CASE II.—F. F., purulent meningitis. Large amount of fluid present. A few areas of purulent exudate over the frontal lobes. Fluid in ventricles slightly increased and cloudy. Bronchopneumonia and edema of both lungs, particularly the lower lobes. Small amount of slightly turbid fluid in the pericardium. Parenchymatous changes in the kidneys.

CASE III.—L. D. Basilar meningitis. Congestion and edema of both lungs.

Although this series does not comprise very many cases, yet the study of them has been of the greatest interest. The chief factor in regard to the prognosis is the period at which the treatment is begun. Under the conditions of civil life these cases are more likely to remain under

observation for a day or two before the diagnosis is made and treatment instituted. At present when the probabilities of a case being meningitis are very great the cases come to the hospital much earlier. In fact, the suspected cases have outnumbered the true. The principle followed has been that it is much better to make a lumbar puncture and get negative results than to overlook a case. A number of patients showing well-marked symptoms of meningeal irritation have proved negative so far as meningitis is concerned, but several on further examination have shown the presence of pneumonia.

The treatment has been instituted in practically all the cases, just on the gross appearance of the fluid without waiting for any further confirmation of the diagnosis. It has also been evident that the conditions of the patient at the time of admission was not always a reliable ground on which to base the prognosis. Some of those who were in well-marked coma came out more rapidly and returned to normal more quickly than others who at first seemed less severely attacked.

As has been the experience generally, those who have recovered after receiving the serum treatment have remained entirely free from any sequelæ. Those who have been discharged as cured have not had a trace of any trouble, no interference with vision or hearing, nothing other than the general weakness following any severe disease.

In regard to the source of infection very little, in a way, has been determined. Eleven of the cases were received from two companies of two regiments that came to the cantonment from an infected section. In about a month it was apparently quiescent in these troops, then after a period of ten days another case developed, but for the past month there have been no further cases. Other cases were much more sporadic, coming from various regiments and companies scattered all around the Camp. In the case occurring in a nurse it was found that she had been taking care of a patient who subsequently developed meningitis. It is interesting to note, however, that both she and the patient developed the disease at practically the same time.

In conclusion it would seem that the important points are:

1. Early diagnosis.
2. Prompt treatment.
3. Persistent treatment.
4. Symptomatic treatment. Control of convulsions by bromides and chloral. Heart stimulants such as digitalein, strychnin and atropin also were used.

AMERICAN JOURNAL OF CARE FOR CRIPPLES.

THE current number of the *American Journal of Care for Cripples* maintains the level of war interest established by its predecessors since inauguration of the policy to include consideration of the military phases of the subject with which it deals.

THE FRENCH SYSTEM FOR RETURN TO CIVILIAN LIFE OF CRIPPLED AND DISCHARGED SOLDIERS. An important and substantial contribution in this issue is that by Major John L. Todd, C. A. M. C., under the above title. Major Todd takes pains to emphasize that the information at his disposal has been obtained from men or commissions

entrusted with such work rather than from the titular heads of departments and considers at some length the methods followed by the French in returning the men discharged from the army to civilian life. He emphasizes also that these methods have by no means reached a final form and are divided in general into the following stages:

1. Active medical and surgical treatment.
2. Functional reëducation.
3. The provision of artificial appliances.
4. Professional reëducation.
5. Establishment in civilian life.

It seems that, for military purposes, the French territory is divided into twenty-one regions, each having an organization complete in itself, and this general structure forms the basis of arrangements for the return of soldiers to their homes. It is estimated that about 30 to 40 per cent. of the French Army will at some time or other be admitted to hospitals established under this plan because of wounds or disease. In addition to general hospitals and those intended for particular purposes the greatest importance is attached to the orthopedic centers, of which there is one in each of the above army regions.

Major Todd's article makes no attempt to consider medical or surgical matters in details, but a few interesting statements are made such as that to the effect that in the orthopedic hospitals above mentioned the stump of every patient having suffered amputation is radiographed on admission. By these means exostoses have been found to be very frequent, especially in the femur often causing a painful stump. It has been found inadvisable to remove them at once because of the possibility of lighting up an otherwise dormant infection by such activities.

Proceeding to the topic of Functional Reëducation, Major Todd places brief emphasis upon the fact that work properly selected and graduated, has not only a high psychic value in men of lowered morale, but also constitutes the best possible means of reaccustoming muscles to action. Incidentally he remarks that many of the nurses and volunteers giving massage and other treatments to such patients have little technical knowledge and that steps are being taken to remedy this by proper instruction.

Under Artificial Appliances the point is brought out that for purposes of uniformity these are to be issued at only six centers in France, together with the admission that the modern aim of an artificial appliance should be to remedy the physiological and not the anatomical loss. Interestingly enough one of the best wooden legs examined by the commission was made for himself by a young joiner and advantage is taken of individual inventiveness and experience in such instances.

It is the intention in France that each man who has suffered amputation shall be eventually supplied with two artificial limbs, one to be held in reserve and it is also noteworthy that laboratories and workshops have been established, not only for the manufacture but also for the devising of artificial appliances, such as those, for example, at Bordeaux and Lyons.

Major Todd proceeds to the other component phases of his large topic and calls attention to the importance of the selection of suitable occupation for disabled men, emphasizing that such choice must not be lightly made, as the "mutilé" is not always capable of deciding

properly. Considerable space is devoted to a survey of this field, including consideration of the blind and deaf. Establishment in civil life is also considered, and Major Todd makes the interesting statement that large numbers of men are being trained as manufacturing orthopedists at the centers of rééducation, and further states that it is well that this is so because already, ironically enough, German manufacturers of artificial limbs are sending out circulars to obtain business in France. The author believes that the many industries under way and planned will do away with the long-established necessity for Old Soldiers' Homes after the war is over, although there will inevitably be a small number of discharged soldiers receiving pensions but incapable of looking after themselves entirely.

Pensions and insurance are taken up in detail, which need not figure in this review, together with the means necessary to meet them. An interesting section is that on Tuberculosis. From a military point of view a soldier is deemed unfit for service when discovered to be tubercular. Although it is plainly the desire of the administration that rulings in this connection shall be liberally interpreted, it is clear that the State should be held liable for disease only in proportion as that disease is demonstrably due to service. There is obviously room for injustice in carrying out such intentions, and tubercular soldiers are usually discharged without a pension.

To date thirteen so-called sanitary stations have been established and twelve more are about to be opened, with the expectation that about 10,000 patients can thus be cared for yearly. The object of these sanitary stations is not to treat tuberculosis but to teach patients how to live so as to avoid infecting others. The duty of caring for these dependents will fall upon the civil and not the military power, and from the nature of their functions most of these sanitary stations will disappear soon after the war's end.

Major Todd remarks that although Germany has forbidden publications concerning prosthesis and functional rééducation, nevertheless considerable information has leaked out and is available to students of the subject.

Another interesting caption in the present article is that devoted to the French nursing system. It seems that before 1903 nine-tenths of the French nursing was done by nuns, and while the school established for this purpose at Salpêtrière, upon Governmental disruption of religious congregations, produced many good nurses, some were not of the desirable type. It appears that the number of highly trained professional nurses in France is less than that now available in Canada, but, on the other hand, the number of women having received some training is considerably larger, owing to the organized dispensary system under which French women, in theory at least, are trained for hospital service in the War analogously to the military training of men. Two types of nurses result, the first being the *Infirmière*, and the second the *Infirmière-Surveillante*, representing an intermediary and final degree of proficiency along the lines of nursing. A diploma for the latter requires two years of service. It is stated that 12,000 women holding diplomas from the *Secours aux Blessés Militaires* are now at work in French hospitals, in addition to which about 10,000 women members of the society are employed in the hospitals as assistants.

A brief summary concludes the article, with emphasis on the belief that private benevolence should play no role in providing advantages which disabled men should receive as a right from their fellow-citizens. In correlating French experience with Canada's needs the author says that the Canadian Army Medical Service, already responsible for establishing the physical condition of a man on his entrance to or exit from the forces, should bear all responsibility of controlling (though not of giving) medical treatment, active or reëducational, until the recipients are discharged or granted pensions.

Nearly half of the final section of this article is in the form of appendices, referring to the various subdivisions of the subject, which contain valuable references to schools, hospitals and other institutions, together with some statistical tables and bibliography. Explanatory comments are attached in many instances to the topics considered.

THE ORGANIZATION AND AIMS OF THE ORTHOPEDIC RECONSTRUCTION HOSPITAL. This very interesting article is by Dr. Mayer, an American surgeon who was connected with the Red Cross Base Hospital Ambulance at Berlin and returned to this country upon the declaration of war. A recital of his views and experience is therefore of particular interest.

Dr. Mayer divides the injured men constituting the homeward bound cripples as follows:

1. The blind.
2. Those suffering with internal diseases; tubercular, non-tubercular, such as chronic heart and kidney diseases, et cetera.
3. The mentally deranged.
4. The group whose motor functions are impaired.

The present paper deals exclusively with the last class. On the basis of two and a half years' experience as chief surgeon to a 500-bed base hospital near Berlin he suggests the following main groups of injuries falling within this last class:

1. *The Amputated.* At the end of 1916 the number of German soldiers with leg amputations alone was 16,000. Dr. Mayer points out that after an amputation the subject is not ready for discharge from the hospital as soon as the wound is healed. The stump must be hardened by proper exercises and reduced to a constant size before an artificial limb can be fitted.

2. *Bone Injuries.* Under this he emphasizes the frequency of improperly set fractures and delayed union.

3. *Lesions in and about the Joints.* The joints may be completely obliterated by a fusion of the bones one to another or they may be stiffened by a long-continued immobilization. In the first type brilliant results apparently follow plastic operations, in which a new joint is formed by chiseling the bones apart and inserting a pad of fat or fascia.

4. *Nerve Injuries.* Rare in times of peace, these constitute a common occurrence in military surgery. The injury is usually a complete severing of the nerve and operative procedures to restore continuity form only the first step in a lengthy course of treatment, many months being required "before the fibers grow from the point of suture down to the muscle which they control."

5. *Tendon Injuries.* Dr. Mayer points out that with the present ample opportunities for studying cases much knowledge has been gained in regard to anatomical and physiological repair along these lines.

6. *Static Deformities.* He also states that, despite rigid examinations, many deformities develop in soldiers owing to the tremendous strain upon their feet, calling for the greatest care on the part of trained orthopedists. An important fact brought out by his experience is the injury which is sometimes produced by indiscriminate and unscientific massage and so-called physiotherapy. He thinks that this work should not be relegated to the hands of a masseur or physical culture teacher.

It is interesting to note that until the war there have been relatively few advances in connection with artificial limbs, the trade having been handed down from one "master" to another, with little or no change. In Germany the Society of Engineers offered a prize for the best artificial hand and arm, as a result of which some unique types were discovered, such as the artificial hand invented by an untrained peasant, August Keller. In the opinion of Dr. Mayer this is unquestionably the best form of prosthesis for the farmer. Dr. Mayer thinks that the possibilities of development in this connection by the Yankee mind are very great.

In concluding the article the author indicates the importance of properly selecting the personnel for hospitals engaged in such work. With the selection of the chief orthopedic surgeons rests success or failure. He must be a master of his art and must also possess a social conscience for the individual needs of his patients. Appended is a table giving the list of personnel for a 500-bed hospital. Dr. Mayer emphasizes what has been so repeatedly brought out, that neither private charity nor haphazard local organizations must be allowed to take care of these men. The responsibility for their care must rest upon the State.

THE RED CROSS INSTITUTE FOR CRIPPLED SOLDIERS AND SAILORS. Mr. Devine outlines the program of the Red Cross Institute for Crippled Soldiers and Sailors, inaugurated by a contribution of \$50,000 from Mr. Jeremiah Milbank, of New York City, who also put at the disposal of the Red Cross the building at 23d Street and 4th Avenue, originally occupied by the College of Physicians and Surgeons. It is understood that the institute will begin its activities where the surgeons and orthopedists cease theirs, and will concern itself with the question of vocational reëducation. A preliminary investigation is being made to cover the work accomplished to date elsewhere, and includes visits to France, England and Canada. Any definite outline of the plans of the institute at the present time would be premature, but it is clear to Mr. Devine that the program must include a study of the needs and abilities of the individual man by medical, educational and social experts. There must be opportunities for learning a great variety of occupations and methods for placing men when they are qualified to accept positions. It is evident that the development of this institute will be along ambitious lines, which will doubtless be followed with the greatest interest.

VOCATIONAL SCHOOLS FOR WAR CRIPPLES IN FRANCE. Under this title is presented an interesting summary of the activities of various schools for this work, including those at Paris, Bourges, Bordeaux and elsewhere: Current Notes on the Organization of After-care for War Cripples in Germany and War Cripples at the Agricultural Training Station, Gross-Tarpen, near Graudenz, Germany.

Two short articles of interest are those bearing upon the care of war cripples in Germany. Nothing particularly new is advanced, but the text is of interest because representing conditions in Germany of which we ordinarily hear little. It is at least developed in these articles that provisions existing on paper for the care of such dependents are not necessarily equally developed in actuality.

To quote the article:

"Practically every village in, say, the Province of Brandenburg flourishes a shingle with a red eagle and the inscription 'Kriegsbeschädigtenfursorgestelle' (war cripples' welfare bureau), but in most cases the posting of the decorative placard is as far as the work of the welfare bureau goes. Things are no better in most of the other provinces.

"The Reichsausschuss für Kriegsbeschädigtenfursorge (federal committee for war cripples' welfare work) has provided for the task in question a great working program on thoroughly commendable basic principles. All of these presuppose the coöperation of an extensive circle of agencies. But the mass of the people, and most particularly the war cripples themselves, can place their confidence in this organization only if all the industries work together, and more particularly the labor interests are adequately represented.

"As a rule, individual war cripples, upon discharge from military welfare agencies, come into contact with the local business offices only, usually the civil war cripples' welfare bureaus. The chief purposes of the latter are vocational guidance and placement in a suitable and remunerative position. The latter task is at present comparatively easy, since work can now be provided for men who retain only half their working capacity—or even less. But things will be different after the war, when, upon the return current of healthy workers with full working powers, war cripples will have to compete with sound men in the daily struggle for existence. Then the lack of a centralized welfare organization will become a calamity with most serious consequences."

R. P.

The Technic of the Carrel-Dakin Treatment.—McCARTNEY and MEWBURN (*British Med. Jour.*, February 9, 1918) describe especially those details which have been introduced into the procedure during their year's experience with it. The solution is prepared daily in the dispensary according to the method of Dr. Daufresne as set forth in the circular of the laboratories of the Rockefeller Institute at Compiègne, issued December 15, 1917. The potassium permanganate is added after the solution reaches the ward, and the amount is 5 mg. to each liter of Dakin's solution. The strength of the hypochlorite should not be over 0.485 per cent., as stronger solutions often cause the wounds to develop a scalded, white appearance. A series of tests was made to see the action of light on the solutions. It was found that if the bottles containing the fluid are kept covered with bags of heavy duck impregnated with a brown floor stain the solution will retain its potency for forty-eight hours. The disinfection of the Carrel tubes and the preparation of the vaselin pads are most important. The Carrel tubes after use are syringed out with warm water, scrubbed with a brush, soaked all night in Dakin's solution, washed off with ether and then boiled for

thirty minutes in a caustic soda solution. In the vaselin pads, cheese-cloth, with twenty-four threads to the inch, gives best results. When the method, which is given in detail, is followed the resulting pads are thoroughly impregnated and adhere perfectly to the skin, allowing no Dakin solution to overflow on to the skin. The medical officer invariably should do all the dressings, as in no other way can there be certainty of the technic. It is possible for one medical officer to dress 50 cases a day if other duties are light. As assistants are one nursing sister and two orderlies, one of whom may be an intelligent convalescent patient. Both nurse and head orderly should be fixtures in the ward, as satisfactory team work and thorough asepsis are only obtained by permanent assistants. The duties of each are carefully planned and carried out. The essential point of the dressing technic is that the wounds, tubes and dressings are on no account touched by the hands. Everything is handled solely by clean dressing forceps. The various stages of the dressings are detailed in order. By these methods there have been obtained in the majority of cases most satisfactory and even surprising results.

W. H. F. A.

Dermatology in Connection with the War.—MACLEOD (*Practitioner*, February, 1918) first discusses dermatitis due to the handling of high explosives, such as tetryl, trinitrotoluene and lyddite. The dermatitis produced by these different explosives is practically indistinguishable, though the staining of the skin associated with each may be characteristic; also the explosives differ to a considerable extent in their capacity for being absorbed and for giving rise to toxic symptoms. The irritating properties of tetryl are so great that it is liable to produce dermatitis in a considerable proportion of those working with it. In its powdery form it is most potent as an irritant. In the process of sieving the powder is given off in a cloud, which becomes deposited on the floors, tables, clothes and exposed parts of the skin. It causes a yellow or apricot-staining of the skin and hair, and this is more liable to occur in skins moist with perspiration than in those which are naturally dry. The dermatitis usually comes out within a fortnight after beginning work with the substance. It varies from simple erythema to definite edema or deep-seated vesication, and is associated with itching so distressing as to interfere with sleep. Only exposed parts are usually involved. Eyelids are apt to be severely affected, and may be so swollen, as almost to close the eyes, and there is some accompanying conjunctivitis. Once an attack has occurred the skin becomes so abnormally sensitive that even if the worker is transferred to another department a recurrence may be caused simply by contact with clothes or even with paper soiled with the tetryl. Cases have been met with not only in the workers themselves but even in those living with them, from handling or washing soiled clothes which have been worn in the factory. Symptoms of absorption are, as a rule, absent or transitory. There may be effects from inhalation and swallowing resulting from irritation of mucous membranes of the upper respiratory passages and of the stomach. The dermatitis heals rapidly under simple local treatment when the worker is removed from exposure to the irritant, but lead lotions must not be used. As preventive measures, in addition to cool clean work-rooms, close-fitting clothing, thorough washing of skin after exposure,

the hands may be hardened with methylated spirits and the face protected with a powder of zinc oxide and starch. Trinitrotoluene is a highly irritating substance, given off in the form of a fine dust in sieving or filling canisters and shells, which settles on the operators and insinuates itself beneath the clothing. On the skin it gives rise to a severe form of dermatitis, and by being absorbed may lead to serious and sometimes fatal toxic symptoms. The superficial yellowish staining is especially noticeable in the creases of the palms, but is not so intense as that caused by tetryl. In severe cases of dermatitis, in addition to edema, there is a papulovesicular or bulbous eruption, which on healing is followed by coarse exfoliation. The vesicles and bullæ are apt to become secondarily infected. There is always more or less intense itching. The general effects which may be of a serious character consist of toxic gastritis, toxic jaundice and rarely toxic anemia. In toxic gastritis the high-colored urine contains trinitrotoluene. Some individuals appear immune while others may show the dermatitis within a week after contact with the substance. It is most common in hot weather, and is specially liable to occur if the skin is greasy, for the trinitrotoluene is soluble in oil. As a prelude to treatment all traces must be removed by gently rubbing the skin or hair with ether or oil. Preventive measures are similar to those used in connection with tetryl. Lyddite has an irritating action due to the picric acid it contains, and causes a dermatitis similar to that caused by trinitrotoluene. It gives a canary yellow or greenish staining of the skin. A number of cases of dermatitis has been reported from handling powder from high-explosive bombs dropped in air raids. The writer also relates his experience with the open method of healing burns in hospitals of the Royal Flying Corps. Since the outbreak of the war the treatment of burns has attracted increased attention due to the frequency of burns received in the field from liquid fire and petrol and in connection with aeroplane crashes. The open method in which healing is allowed to take place under a natural scab the writer considers it in some ways preferable to the paraffin treatment. It is particularly useful in burns of the leg and face, especially in the healing of the granulating surfaces after the separation of the eschar. The raw surface is powdered over with a bland aseptic powder. This contains sterilized stearate of zinc or magnesium carbonate, and a sample formula is given. The powder is added from time to time until the scab becomes a coarse, yellowish-green crust, a quarter or half-inch in thickness. In many cases this can be left alone until the wound heals. But should the discharge beneath become excessive it may be necessary to remove a small portion and bathe away the seropurulent fluid and reapply the powder. The method is useful as not necessitating periodical redressings, and leads to the formation of a pliant scar, which has comparatively little tendency to contract.

W. H. F. A.

The Nutritive Value of Straw Treated with Alkali in the Dietary of Man.—RUBNER (*Arch. f. Physiol.*, 1917, p. 339) states that straw treated with alkali and then used as a diluent for bread when given to man increases the nitrogen and energy loss in the feces to a greater extent than it could furnish either to him.

G. L.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica and Diagnosis, Jefferson Medical College, Philadelphia. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. IV, December, 1917, and Vol. I, March, 1918. Philadelphia and New York: Lea & Febiger.

THE last volume of *Progressive Medicine* for 1917 appeared in December. The first 115 pages is given up to an exhaustive review of the most recent advances in diseases of the digestive tract and allied organs, the liver, the pancreas and the peritoneum. Dr. M. E. Rehfuss discusses in this article the recent literature on the above subjects, including diseases of the tongue and mouth and of the esophagus and stomach, to the latter of which he devotes by far the greater part of his contribution. His discussion is full and interesting and should be useful to the general practitioner. Dr. J. Harold Austin then follows with a discussion of the literature on diseases of the kidney. This review deals with renal physiology, experimental nephritis, the renal functional tests, uremia and acidosis, and the remainder of the article is devoted to nephritis, including trench nephritis, ureteral obstruction and the renal function in pregnancy. He concludes his contribution with an article on the diagnosis of renal tuberculosis. Dr. Charles W. Bonney then discusses genito-urinary diseases, including the surgical conditions of the kidneys, diseases of the bladder, the penis and urethra, and then follows a review of the literature on military surgery by Dr. Joseph C. Bloodgood.

Those who are familiar with the admirable review on surgery that Dr. Bloodgood has contributed for many years to *Progressive Medicine* will welcome the critical review on military surgery that this author has written for the December number of this journal. At a time when so many of the medical profession of this country have entered or are about to enter the military service it is of vital importance that they should thoroughly understand the great problems that are confronting the Medical Department of the Army.

He begins by calling attention to some of the most useful new books on military medicine and surgery, and then points out the wonderful opportunities for special training and education that the Surgeon-General of the Army has so wisely provided for medical officers.

Shock is an important factor in the ultimate prognosis of the wounded, and Dr. Bloodgood deals with this subject at considerable length. He cites the opinions of those who have had the best opportunity to observe the condition of shock as it occurs in and near the trenches; discusses the role played by cold, fatigue, painful dressings and rough transportation in its production and gives valuable suggestions for combating it.

After touching on shell-shock, he digresses and takes up in detail first aid as applied to industries, a subject of greatest economic importance in peace as well as in war, and one in which he has always taken an ardent interest.

Much uncertainty exists in the minds of many as to the exact disposition and duties of the various units of the medical department in combat. This entire subject is well handled, with unusual clearness, by the reviewer. As the basis of his discussion he avails himself of the several articles and notes that have recently been contributed by Colonel Goodwin, of the British Royal Army Medical Corps along this line. In his review, Dr. Bloodgood notes the steps necessary for the transportation of the wounded from the firing line back to the base hospitals. He also takes up in detail the organization, equipment and duties of the different medical units operating in the zone of the advance as well as those on the line of communication and at the base. The comparison which he draws between the disposition of the British medical personnel in the theater of operations and that employed by our own army is most helpful and instructive. He also comments at length on many valuable statements and suggestions that Colonel Goodwin has made from time to time on shock, wound treatment, gas gangrene, fractures and their treatment at the front, abdominal wounds, trench-foot and gas-poisoning. He also reviews the question of first aid in war, especially in the trenches, and the first-aid packages of the English and American armies. This involves a discussion of the mooted question of the use of iodine by the soldiers themselves. The weight of evidence is against its routine use by the unskilled.

The most striking feature of Dr. Bloodgood's contribution is his plea for the universal adoption of the Carrel-Dakin treatment of infected wounds. He describes the wonderful hospital for the treatment of wounds by the Carrel-Dakin method that has been established by the Rockefeller Institute, where, under the guidance of Carrel himself, Medical Reserve Officers are instructed in all the details of the method.

No less important is Dr. Bloodgood's account of military ortho-

pedics in its broadest sense. No one has done more to develop this branch of surgery than Colonel Robert Jones, of Liverpool.

There is no part of Dr. Bloodgood's article more generally useful to officers of the Medical Reserve Corps than that which deals with the soldier's feet, and more particularly with flat-foot, its diagnosis, significance and management. Like most writers on this subject he is lavish in his praise and approval of the United States Army shoe devised by Colonel Weimer.

Under Surgical Bacteriology Dr. Bloodgood expresses the hope that the antitoxin for the gas-bacillus infection discovered by Carroll G. Bull will prove as efficacious in combating this dread infection in human cases as it has in animal experimentation.

In conclusion he outlines the extensive plans that are being made for the reconstruction and reëducation of the large number of wounded that must inevitably result from this war.

It would be difficult to find a more complete, concise review of the essentials of modern military surgery than is embodied in Dr. Bloodgood's article? It has the added advantage of being replete with illuminating comments based upon the extensive surgical experience of the author. The medical officers, and particularly the Medical Reserve Officers, who fail to avail themselves of this contribution by Dr. Bloodgood, seriously neglect a timely and valuable educational opportunity.

The concluding 97 pages of this volume contain a discussion of the newest achievements in practical therapeutics by Dr. H. R. M. Landis, who takes up at considerable length the latest advances in this line, and in his usual interesting and enlightening way brings to our notice the literature on adrenalin, alcohol, ammonium chloride, asperin, camphor, etc.

Vol. I, 1918, opens with an article of 92 pages by Dr. C. H. Frazier on surgery of the head, neck and breast, and deals largely with war surgery of these parts. He discusses the literature on gunshot injuries extensively, and concludes with surgery of the mammary gland. Dr. George P. Müller then follows with a review of the surgery of the thorax, including diseases of the breast, and the larger part of his article also deals with war surgery. Dr. John Ruhräh then discusses in his usual interesting and exhaustive way the literature on infectious diseases and gives an abstract of what the Rockefeller Foundation has done with war relief work in China with hookworm disease and the Yellow Fever Commission in South America. He calls attention to the value of flavine and brilliant green as antiseptics and to the keeping qualities of therapeutic serums. He then takes up the subject of dysentery carriers, bronchial asthma, cerebrospinal fever, the skin reactions in infectious diarrhea, Hodgkin's disease, hookworm disease, epidemic nephritis, and devotes 27 pages to the subject of poliomyelitis. He discusses trench fever and trench-foot, typhoid and typhus fever, Weil's

disease, and concludes with an article on whooping cough. Dr. Floyd M. Crandall refers to the advances in diseases of children, particularly the effect of civilization upon children's diseases. He then in turn discusses the diathesis in childhood, acidosis in children, luetic nephritis in infancy and childhood, the influence of vitamins, stenosis of the pylorus, chorea, chronic intestinal indigestion in children, and concludes his article with ten pages on infant-feeding, including a table of food allowances for children under two years up to seventeen years. The volume concludes with an article of 82 pages by Dr. George M. Coates, who devotes this space to the more recent advances in rhinology, laryngology and otology, giving particular attention to the military phases of these subjects. The volume, though not as large as usual, is complete, and should prove both interesting and useful to all medical and surgical men.

S. S.

A POCKET FORMULARY. By E. QUIN THORNTON, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College, Philadelphia. Eleventh edition. Pp. 292. Philadelphia: Lea & Febiger, 1918.

THAT there is a broad and legitimate field of usefulness for works of this character is self-evident, though it is not at all meant to replace individual thought on the part of the practitioner. Even the best informed physicians may at times overlook an appropriate drug or combinations that make for palatability and pharmaceutical elegance.

This *Formulary* serves its purpose well, and in revising the author has enhanced its value by signifying the indications as to the use of each formula.

C. N. S.

HUMAN PHYSIOLOGY. By PROFESSOR LUIGI LUCAIANI, Director of the Royal University of Rome. Translated by FRANCES A. WELBY. Vol. IV, The Sense Organs. Pp. 519; 217 illustrations. London: Macmillan & Co.

THIS volume deals with the physiology of the sense organs, and contains chapters on cutaneous sensibility, sensibility of the internal organs, taste, smell and hearing. Three chapters are devoted to the visual apparatus under the headings Dioptric Mechanism of the Eye, Retinal Excitation and Visual Stimulation and Ocular Movements and Visual Perceptions. The final chapter deals with the psychophysical phenomena of consciousness and sleep. In each of these subjects numerous researches are discussed and the points of view and results of the investigators are reviewed in detail, while here and there the author gives his own opinion to illumine the path

of the reader. A book written on this plan excels not in giving general results but in showing, by tracing the growth of our knowledge, how present-day conceptions have been reached. This historical analysis is at once the most interesting and the most elusive side of the study of a science. To use this form of presentation necessitates many detailed descriptions, but it is the distinctive achievement of this book that it is eminently readable in spite of the minute details often entered into. Considering the experience and reputation of the author and his long scientific career, one may regard the views assembled here as those most tenable in the light of present knowledge and of lasting value, because necessary for consideration in any further progress of the science.

W. H. F. A.

LORD LISTER. By SIR RICKMAN JOHN GODLEE, BT. Pp. 676; 33 illustrations. London and New York: Macmillan & Co.

IN these days of warfare and military surgery, when the treatment of infected wounds and the study of new antiseptics become of supreme importance, one is brought back vividly by this book to Lister's early day, when he began to deal with the ever-present foul wounds in civil hospital practice. Problems similar to those which he sought to solve present themselves under a somewhat different form, and after the interval of years, in which the modified form of antiseptics known as asepsis has been to the fore, we find the search for methods of antiseptics demanding increased attention.

This life of Lister, interesting as the record of a personality, is still more important as a contribution to our knowledge of the working out of a great idea. The author, a nephew of Lister, lived for many years in close personal contact with him, associating with him, both in the hospital wards and in the laboratory, so that he was well fitted for the task of biographer. In keeping with Lister's expressed desire it is chiefly a record of what he accomplished for science and for surgery, but we are also shown many glimpses of his daily life without which such a record would be incomplete. After reading of Lister's scientific activities, one may safely conclude that he would have made his mark in whichever branch of science he might have chosen to follow. Throughout his life he combined creative laboratory work with the practical problems which he sought to solve. Acquainted with microscopy from his earliest years, when his father was engaged in making great improvements in the lenses of the microscope, he used this instrument successively in normal histological, physiological, pathological and bacteriological studies, and in all of them he contributed something of value. Perhaps the most interesting part of the book is that dealing with the events leading up to his first successful treatment of a case by

the antiseptic method, using carbolic acid. This was in 1866, and this represents the beginning of his search for and study of new antiseptics, which continued practically to the end of his life. To everyone interested in the progress of medicine this volume will be of lasting value, constituting, as it does, the record of a great man who accomplished great results.

W. H. F. A.

A TEXT-BOOK OF OBSTETRICS. By BARTON COOKE HIRST, M.D., Professor of Obstetrics in the University of Pennsylvania. Eighth edition, revised. Pp. 863; 715 illustrations. Philadelphia and London: W. B. Saunders Company, 1918.

IN bringing forth the eighth edition of this valuable practical book the author has revised the text so that the subject matter has been brought up to date and due attention has been given to all of the worthy additions to the art of obstetrics that have been presented to the profession since the last revision of the book six years ago. There is little that a reviewer can say about a book of this kind that has long since become a favorite in the average medical library. While it is hardly so complete and exhaustive as one or two other text-books on the subject that have been presented in recent years, it is pleasing to note that the author is continually revising it, so that the book can always stand on its own merits rather than being obliged to depend on its early editions for its prestige. The literary style of the author, together with the many amusing anecdotes that are used by way of illustration, serve to make the text very pleasant reading, and one that should specially appeal to the medical student.

F. B. B.

THE TECHNIC OF THE IRRIGATION TREATMENT OF WOUNDS BY THE CARREL METHOD. By J. DUMAS and ANNE CARREL. Translated by ADRIAN V. S. LAMBERT, M.D., Acting Professor of Surgery in the Columbian University. Pp. 81; 11 illustrations. New York: Paul B. Hoeber, 1917.

THIS small book was written by Madame Carrel primarily for nurses, in order that they might have a clear, short account of the various details of the technic and an accurate description of the apparatus used in carrying it out. An appreciative introduction is furnished by the noted and still active American surgeon W. W. Keen. Those wishing to become proficient in the employment of this method of treatment will find this book devoid of confusing theoretical considerations. The stage of discussion concerning the value and importance of this new way of handling infected wounds having passed we are prepared to welcome such a brief, complete and authoritative treatise on the subject.

T. T. T.

PROGRESS OF MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Volkman's Ischemic Paralysis and Contracture.—TAYLOR (*Ann. Surg.*, 1917, lxxv, 28) says that experimental work and clinical observation point to traumatic myositis as the fundamental condition in causing Volkman's ischemic contracture. The pressure causing the muscle disorganization is both internal and external: internal because the flexor muscles are firmly confined by their envelope of aponeurosis and bone, and external because of tight dressings or the position of acute flexion of the elbow. The degenerated muscle substance is replaced by connective tissue, the contraction of which causes the typical deformity. The damage to the muscle may be very slight, it may be complete, or it may be of any grade between these two extremes, and it is impossible clinically at an early time to determine just how extensive the damage is. Pressure sloughs and abscesses are common on the ulnar side of the wrist and on the flexor prominence just below the elbow. When present these abscesses usually burrow to the deeper structures, heal very slowly and add greatly to the cicatricial rigidity. Nerve injury is purely a complication. It occurs in about 60 per cent. of the cases. It may be primary as the result of the accident, or secondary as the result of the pressure of the swollen muscles, or occur, more frequently, later as the result of cicatricial constriction. The ulnar and median nerves are most often involved and are usually constricted a short distance below the elbow. The prognosis should, as a rule, be unfavorable. Inasmuch as it is impossible to determine clinically the exact amount of damage, an accurate prognosis can not be given until the reaction to proper treatment has been watched for a time. In children from one to fourteen years of age, in injuries about the elbow region, tight dressings should be avoided, as well as extreme flexion of the elbow. All cases should be watched for undue pain, swelling and cyanosis, so that prompt measures may be taken, if necessary, to prevent the full development of the lesion. If in spite of these measures

the swelling and cyanosis increase, one should attempt decompression of the flexor muscles by splitting the deep aponeurosis longitudinally, either subcutaneously or together with the skin if that is edematous and shiny. Late operation is done either to lengthen all the tendons of the contracted muscles to permit simultaneous extension of the fingers, hand and wrist to a straight line, or to shorten the bones sufficiently to attain the same result. After an operation has mechanically relieved the deformity, the real work of rehabilitation must be done by a prolonged course of physical therapeutics. Therefore it would seem preferable to avoid the trouble and risk of operation by employing the method of mechanical overstretching of the contracted tissues. This method combined with physical therapeutics obtains results which for promptness and quality are as good or better than those obtained by operation. This may be accomplished by the Jones method of rigid splints or by the method preferred by the author, which may be called the elastic traction method. Persistence in treatment is the only hope of success in the severe cases.

Enterostomy for Ileus.—DOUD (*Ann. Surg.*, 1917, l xv, 95) says that the operation of enterostomy is a very old one, at least one hundred and twenty-nine years. It is resorted to now much more frequently than it used to be. The details of the procedure differ with the case. Sometimes, without anesthesia, a little opening is made in a loop of the intestine which presents in the drainage wound; sometimes under local anesthesia, a small abdominal incision, a catheter or small tube, is tied or stitched into an opening in the intestine, and a few Lambert stitches secure the intestine to the abdominal wall; sometimes, under general anesthesia, a search is made for a definite obstruction, and failing to find this, an enterostomy opening is made with careful provision for the subsequent closure of the wound. Sometimes at the termination of a primary operation in unfavorable cases, an enterostomy is done as a safeguard. In all cases the stoma should be as small as will be efficient. Nothing in surgery is more dramatic than the improvement which comes from a fortunate enterostomy. A patient who is almost moribund before the operation is, a few hours later, comfortable, bright, and hungry. The obstruction is frequently temporary. If there are many angulations in a moderately inflamed intestine, the total obstruction may be sufficient to produce stasis. Such obstruction, however, ceases if the distention can be relieved, and if the inflammation subsides. In closing the opening later, Doud loosens the intestine from its adhesions to the abdominal wall, but a very wide exposure of the peritoneum is avoided. Through-and-through stitches invert the edges of the intestinal stoma. Lambert stitches reinforce the suture line, and almost complete closure of the abdominal wall, in layers, has followed. This closure has not been absolutely complete, as provision has always been made for drainage at a little distance from the intestinal sutures. Intestinal resection is a severe operation and is to be avoided when possible.

Fatal Complications of Percy's "Cold Iron" Method in the Treatment of Inoperable Carcinoma of the Cervix.—LEONARD and DAYTON (*Surg., Gynec., and Obst.*, 1917, xxiv, 156) says the

Percy method consists in the application of long-continued low heat in the treatment of otherwise inoperable carcinoma of the uterus. This procedure is based upon a principle claimed by Percy, namely, that carcinoma cells are killed by low penetrating heat insufficient to destroy normal tissues. The Percy method has been widely adopted and the results so far reported have been almost uniformly favorable. He summarizes his observations and full reports of two fatal cases treated in the Gynecological Clinic of the Johns Hopkins Hospital. The primary effect of the Percy cautery is to cause a necrotic mass extending more or less uniformly in all directions from the coagulating point. A mass of sloughing coagulated tissue of this type offers an ideal medium for the growth of microorganisms. It will probably be found impossible to prevent infection of this area, and once infected the thrombosed vessels of the region may offer a ready entrance into the system. Therefore the danger of a septicemia is considerable. The authors are convinced, from their short experience with Dr. Percy's method, that fatalities must have been frequent wherever this method has been employed extensively, yet they were able to find only one complete report of a fatal case in the literature, that of Dr. Boldt. They conclude that the prolonged treatment of large carcinomatous masses by low heat may result in a rapidly fatal outcome with lesions similar to those in cases of fatal cutaneous burns. The necrotic mass produced by the cautery forms a particularly favorable medium for bacterial growth. The organisms may spread to the surrounding tissues or reach the general circulation through the local thrombosed vessels. It seems probable that the greatest danger in the application of the Percy cautery is a local infection and a subsequent general sepsis. Finally, the technic is ineffectual in eradicating the carcinoma. There is no evidence from these two cases that carcinoma is more susceptible to heat than is normal tissue.

Observations on Gas-bacillus Infection in France. — JUDD (*Surg., Gynce. and Obst.*, 1917, xxv, 113) says that of all the classes of wounded seen in the present European war the most terrible and formidable are those of the so-called gas-bacillus infection. Modern trench warfare with the accompanying difficulties in providing cleanliness exposes a large proportion of wounded to the dangers of gas-bacillus infection. The majority of cases follow shell wounds when a piece of contaminated clothing is carried into the depths of the wound by the projectile. Among the varieties of microorganisms present in the wounds, the bacilli perfringens are generally accepted as the causative organisms. These bacilli appear in the wound from the ninth to the twelfth hour. The aerobic bacteria appear about the forty-eighth hour. The symptoms of the infection appear early, usually on the second day. The parts of the body most often affected are the legs on account of the likelihood of their becoming contaminated by dirt and fecal matter. It is of vital importance that the diagnosis be made early. Pain, swelling and tension of the wound with rapidity of the pulse are important early symptoms. Vesicles, discoloration of the skin, gas formation and odor should be considered later symptoms. The prognosis depends on whether the patient receives proper early treatment. Trench hygiene and personal cleanliness are vital prophylactic measures.

Early incision of the wound with removal of the foreign bodies, cleansing of the wound and excision of damaged tissue doomed to slough are the correct surgical procedure of prevention. When the infection is once established, well placed, deep incisions exposing the deeper tissues to the air, are indispensable. For the clinical treatment of the wound, Dakin's solution has given the best results. Amputation must be resorted to in many cases and should not be delayed beyond the proper period.

Intrapericardial Traumatic Hemorrhage.—RHODES (*Ann. Surg.*, lxvi, 1917, 44) says that in general very few traumatic lesions of the thorax demand operative relief. But there is a definite type of thoracic injury in which interference must be prompt, and no considerations such as the critical condition of the patient must interfere with such operative attack. This refers to acute hemorrhage of large amount into the pericardial sac, accompanied by very slight opportunity for the free outlet of the hemorrhage. Rhodes operated on 2 cases. The first was a stab wound of the pericardium with intrapericardial hemorrhage. A rectangular osteoplastic flap was made in the following manner: An incision was made over the middle of the sternum, extending from the second to the fifth costal cartilages. From the upper and lower ends of this, incisions were made at right angles to it for a distance of five inches. This skin and muscle flap was dissected back and the cartilages of the third and fifth ribs were divided subperichondrally. The fourth was already divided by the injury. The intercostal spaces were then divided and the whole osteoplastic flap bent backward, breaking the ribs, probably at the junction of the cartilage and rib. The internal mammary artery was ligated. This gave splendid access to the anterior mediastinum. The triangularis sterni was incised and pushed aside, the pleura was seen to lie very close to the left sternal margin, and the rent was seen where the knife had penetrated. When the pericardium was opened a tremendous gush of blood came out, apparently under tension. No stab wound of the heart was found, the source of the hemorrhage being found to be a large pericardial vessel. This was ligated and the field remained dry. The wound was closed without drainage, the pericardial sac being previously washed out with salt solution. He left the hospital nineteen days after admission with a perfect cosmetic result. Heart and lung action was normal. The second case was one of stab wound of the pericardium and right ventricle intrapericardial hemorrhage; and unsuccessful attempt at heart suture. He concludes that in practically all cases of stab wound of the heart an accompanying injury of the pleura occurs, usually, resulting in a pneumothorax. Extreme symptoms of respiratory embarrassment should be considered as caused by the heart tamponade, and not by the pneumothorax alone. The tamponade must be relieved at once. These cases stand ether anesthesia well. The incision used in these cases gives splendid access to the heart and gives perfect functional and cosmetic results. Drainage is not necessary, but the sac should be washed out before closing, preferably with salt solution.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Pharmacology of the Oil of Chenopodium.—SALANT'S (*Jour. Am. Med. Assn.*, 1917, lxix, 2016) experiments on animals (rabbits, cats, etc.), indicate that oil of chenopodium, even in very small quantities, may prove very toxic. He notes that sensitiveness to the oil persists for from five to nine days and warns that the repetition of a non-effective dose within this period may cause serious symptoms or even death. The toxicity of oil of chenopodium varies largely with the nutritional condition of the animal. Fasting or poorly nourished animals succumbed to much smaller doses than did those that had been receiving a carbohydrate-rich diet for sever aldays before the oil was given, or when the administration of oil of chenopodium was preceded by a sufficient quantity of a fatty oil, such as, olive, cocoanut, or castor oil. As regards its therapeutic use, Salant concludes that oil of chenopodium should be used with caution for internal medication as it has a tendency to affect the central nervous system, the heart, respiration, the digestive organs, and the kidneys. In renal or cardiac disorders the oil should be given in small doses only, while in advanced chronic nephritis or heart disease its use would seem to be altogether contra-indicated. As the liver undoubtedly plays an important part in detoxifying oil of chenopodium, while changes in the gastric and intestinal mucosa may accelerate its absorption into the circulation, it may prove more toxic in hepatic and gastro-intestinal diseases. A diet containing a liberal amount of fats and carbohydrates, fed for at least several days before the treatment is instituted, may render the drug much safer. The routine administration of large doses of castor oil before and after the oil of chenopodium may be of prophylactic value. In the treatment of poisoning, Salant recommends gastric lavage since absorption of the oil from the stomach is slow; as, however, absorption from the duodenum is rapid, lavage must not be too long delayed. No chemical antidote to oil of chenopodium has been found; the treatment, therefore, must be symptomatic. Experiments on the isolated heart show that digitalis and epinephrin are excellent antagonists; caffen, on the contrary, appears to increase the toxic action of the oil.

Tartar Emetic in the Treatment of Malaria.—FALCONER and ANDERSON (*Lancet*, 1917, cxviii, 743) treated 8 cases of malaria by the intravenous injection of tartar emetic as suggested by Rogers. Of the 8 cases, 2 were mixed infections, 1 subtertian malaria, and 5 benign tertian malaria, 3 of which showed gametocytes. In the two mixed infections the crescents disappeared in both, the benign tertian parasites persisting in one and disappearing in the other. In the subtertian crescent infection the crescents disappeared after four injections of

tartar emetic. Despite their disappearance the patient had three typical clinical attacks of malaria though the parasites could not again be demonstrated in the peripheral blood. In none of the five benign tertian infections did the parasites disappear from the blood stream until large doses of quinin had been administered. In 2 of the 3 cases where gametocytes were originally seen this type of organism was found subsequent to the tartar emetic treatment. Neither in the subtertian nor in benign tertian cases was any marked clinical improvement noted, and in the benign case the tartar emetic did not appear to exert the slightest effect on the parasite. The results of treatment were so disappointing that the authors do not feel justified in continuing their observations.

Cerebrospinal Fever: The Mode of Infection of the Meninges.—WORSTER-DROUGHT and KENNEDY (*Lancet*, 1917, exciii, 711) admit that the nasopharynx is the primary portal of entry of the meningococcus in cases of cerebrospinal fever. From their clinical and bacteriological study of cerebrospinal meningitis they conclude that the meninges are rarely involved by direct extension from the nasopharynx *via* the middle ear, sphenoidal or ethmoidal sinuses. The usual mode of meningeal involvement is by way of the blood stream. In the ordinary type of cases the coccus is carried to the meninges by the blood within a few hours (usually less than forty-eight) without definitely infecting the blood itself. In these cases the blood stream is purely a carrier, and there is little or no proliferation of the cocci during their transit. In severe cases, however, true blood infection (septicemia) occurs. In the fulminating cases septicemia overshadows the meningitis and at autopsy the meninges show no typical signs of inflammation. In rare cases the organism may remain infecting the blood alone for a considerable time before finally reaching the meninges; or the patient may die of septicemia without showing any signs of meningitis. In other cases the meningococcus invading the blood may also invade structures other than the meninges. In 1 case of meningococcal septicemia the aortic valve showed ulcerative endocarditis and perforation of one cusp. Cocci were demonstrable in the vegetations. The brain was pale and anemic. There was no meningitis. From an analysis of the other cases the authors conclude that catarrhal conditions predispose to meningococcal infection, but the meningococcus does not necessarily produce nasopharyngeal catarrh.

The Red Blood Cell Count and Hemoglobin Content of the Blood in Disordered Action of the Heart.—LEVY (*British Med. Jour.*, 1917, ii, 715) reports the results of a most careful examination of 15 patients at Hampstead Military Hospital. They were unselected cases of disordered action of the heart of all degrees of severity. None of these patients had been "gassed" and none exhibited unusual symptoms, such as nocturnal dyspnea. The average red blood cell count of the 15 patients was 5,008,007. Range: 4,892,000 to 6,600,000. This is quite in excess of anything previously reported in healthy individuals, and is the more remarkable in view of the fact that these men were all invalids who had spent a considerable time in the hospital before the estimation was made. One-third of these patients had a count of over 6,000,000 and 53 per cent. had a count of 5,900,000 or more. The

hemoglobin content was for the most part below the normal 100 per cent., the average being 93.4 per cent. Range: 87 to 100 per cent. The average color index was 0.8. Range: 0.74 to 0.9. No relation exists between the red blood count and the severity of the cardiac disorder. Levy is unable to suggest the significance of this polyerythrocythemic condition.

A Note on Serum Sickness in Cerebrospinal Meningitis.—KERR (*Lancet*, 1917, cxiii, 822) was led to the present study by the fact that of a series of 48 cases of cerebrospinal fever treated with Flexner's serum no less than 76 per cent. suffered from serum sickness. The reactions were, as a rule, quite sharp and in most cases were accompanied by considerable fever. The outstanding feature was, as usual, the rash, which often started as an urticaria and then ran into a multiform erythema. Very severe arthritis was noted in 6 cases; adenitis in 2; in 9 patients a prodromal fever occurred from twelve to twenty-four hours before the appearance of the rash and was accompanied by an exacerbation or relapse of the meningeal signs. More than two-thirds of the reactions commenced on the eighth, ninth, or tenth days after the first injection; the symptoms usually lasted several days. The author points out that the introduction of horse serum into the spinal canal is liable to set up a local reaction which may be described as an aseptic meningitis. A previously clear fluid may become turbid and a slightly turbid fluid may become more opaque. These changes are due to the presence of an increased number of polymorphonuclear leukocytes. When a spinal fluid is so changed the serum reaction and the rash usually follow within a few days, and it appears that a meningeal reaction is a prodromal sign of the more usual phenomena. Kerr finds that Fehling's solution is reduced by all the fluids that become more turbid as the result of a serum reaction. The large number of rashes in this series of cases suggests that the intrathecal injection is more liable to cause them than the subcutaneous. Kerr does not believe that the method of administration is at fault. He ascribes the large number of reactions to some peculiarity of the horses from which the serum is obtained. The occurrence of the rash is not much influenced by the dosage. Kerr believes that many cerebrospinal patients are much improved by these injections and that they are no cause for anxiety. He suggests that the benefit may be due to some stimulus of metabolism or of the processes of repair. He is convinced that in cases which are apparently threatening to enter the chronic stage the improvement which follows serum sickness may be ascribed to the almost perfect counter-irritation offered by the widespread pruritic rash. Kerr does not inject serum in the presence of a serum reaction unless the diplococci in the spinal fluid appear to be increasing. The Fehling test is a useful means of determining whether a rise in temperature with an exacerbation of meningeal symptoms is caused by a serum reaction or by a recrudescence of the disease.

Serum Disease after Intrathecal Injections of Serum.—In this paper ROLLESTON (*Lancet*, 1917, cxiii, 821) compares the manifestations of serum sickness after the intrathecal and after the hypodermic method of serum injection. His conclusions are based on the clinical

notes of 96 cases of proved cerebrospinal fever in the Royal Navy. All of these patients were treated with serums and survived for at least ten days. Out of the 96 cases, 58, or 60 per cent., had a serum reaction as judged by the appearance of the rash. Among these 58 there were 9 (15.5 per cent.) in which the rash was preceded or accompanied by a recrudescence of the meningeal manifestations, suggesting a relapse of the disease. These symptoms were relieved by lumbar puncture, and, under the impression that they did point to a relapse, a fresh injection of serum was given in 6 of the 9 cases. The 3 cases not injected recovered. Of the 6 patients injected intrathecally 4 died. It had been shown by Neal and others that the injection of serum into a healthy or very slightly inflamed intrathecal space sets up an aseptic chemical meningitis, characterized by edema of the meninges, and shown clinically by fever, rigidity of the neck and other signs of meningeal irritation. In a patient with signs of meningeal irritation it is important to be able to decide whether there is a genuine relapse which will be benefited by serum or whether the condition is one of meningism and a manifestation of serum disease which will be intensified by a further injection of serum. The diagnosis between these two conditions can be made by examining the fluid for the presence of meningococci and also for glucose. The latter is absent in true relapses but present in meningism due to serum sickness. Rolleston's statistics at first glance seem to confirm Flexner's statement that meningism is more frequent after intrathecal than after subcutaneous injection of serum. However, Rolleston believes that the serum he used was especially effective in producing a serum reaction, and, from an analysis of his cases, he concludes that the reaction is not more frequent after intrathecal than after subcutaneous injection. In the cases here reported the serum sickness cannot be ascribed to the large quantities of serum employed, for 8 of the 9 cases received less than 100 c.c., and of these 4 received less than 50 c.c. The intrathecal injection of serum necessarily involves some risk of inducing increased intrathecal pressure and may introduce a secondary infection. Rolleston's observations fail to confirm the suggestion of Netter and Salanier that the volume of the serum injected favors secondary infection of the meninges by pneumococci from the blood stream.

The Bruck Precipitin Test for Syphilis.—STILLIANS (*Jour. Am. Med. Assn.*, 1917, lxi, 2015) performed the Bruck test, according to the author's technic, in 209 cases. In 53 of these (over 25 per cent.) the results disagreed with those of the Wassermann reaction. In 13 cases of active early syphilis, in all of which the Wassermann reaction was very strongly positive, the new test was negative. On the other hand, 24 per cent. of 74 non-syphilitics gave positive Bruck reactions. These occurred in 1 febrile case (septicemia) and in 16 afebrile cases, comprising 1 case of gonorrheal urethritis, 1 of gonorrheal arthritis, 1 of xanthoma planum et tuberosum, 1 of systemic blastomycosis, 1 of dermatitis venenata, and in 1 healthy man, 3 nursing and 8 pregnant women, all apparently healthy. Stillians concludes that the Bruck precipitation test for syphilis fails in a considerable percentage of early secondary syphilis and that it gives positive reactions in from 24 to 28 per cent. of non-syphilitics.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Labor Obstructed by Ovarian Cyst.—SALISBURY (*Jour. Obst., and Gynec., of British Empire*, June-August, 1916) reports the case of a multipara who had been six days in labor, with acute pain, the membranes having ruptured two days previously. She was at full term. On admission, strong uterine contractions were present, with signs of exhaustion. Thirty ounces of urine were withdrawn by the catheter. The child was dead and the head fixed in the pelvic brim. A large, tense cyst filled Douglas's pouch completely below the presenting part, and no attempt was made to displace it. The patient was given stimulation and sedatives, and, when her condition improved, operation was performed. A dermoid cyst of the left ovary the size of an ostrich egg was withdrawn from the pelvis with some difficulty and ruptured during its extraction. The cyst was removed, the uterus replaced in the abdomen, and the fetal head pushed into the pelvic brim. The patient was then placed in the lithotomy position, the occiput manually rotated to the front, and a dead child was delivered with axis-traction forceps. The abdominal wound was then closed, and the patient made an uninterrupted recovery. A second case was that of a woman who had been confined to her home by a midwife who felt a mass behind the vagina and the fetal head high up in front, strong pains being present without progress. After some delay a living child had been born and the pelvic mass had disappeared. The patient vomited once and had some abdominal pain. During the day the patient felt comfortable and was sent into the hospital the next morning. On admission she stated that she was comfortable, but the pulse was quick and there was distinct tenderness on deep pressure over the abdomen. The abdomen was opened and serous blood and mucoid material were present. A semi-solid, multilocular cyst adenoma of the left ovary, weighing two and one-half pounds, was found to have ruptured, and one loculus was still lying in the pelvis. The cyst was removed, the fluid mopped up, and a drain inserted. The patient made an uninterrupted recovery. In the third case, as labor commenced, a physician found two polypi in the vagina. On admission to the hospital a small cyst of the left ovary was found to move freely over the left surface of the uterus. A vaginal examination revealed two polypoid adjacent to old scar. Dilatation of the cervix had not commenced. In Douglas's cul-de-sac there was a tense, hard mass the size of a hen's egg, continuous on the left side of the pelvis, with a soft cyst. The mass was immobile and had been diagnosed as a dermoid cyst of the right ovary. Before operation a quantity of liquor amnii escaped through the vagina. When the abdomen was opened the pelvic mass could not readily be approached, so the uterus was first emptied by Cesarean section and a living child delivered. The pelvic

mass was a dermoid of the right ovary, the size of a cocoanut, afterward found to contain bone and teeth. A dermoid of the left ovary was also present above the pelvic brain. Both cysts were removed and the patient made an excellent recovery.

Labor Complicated by Face Presentation.—TITUS (*Surg., Gynec., and Obst.*, December, 1916) writes concerning face presentation in which posterior rotation of the chin into the hollow of the sacrum occurs. He reviews the literature of the subject and quotes a case operated upon by symphysiotomy in 1903. He also describes 2 cases, which have been reported, in which this treatment was carried out. He believes that a reasonable test of the second stage of labor should be allowed to these patients in the hope that anterior rotation will take place. He finds that attempts to rotate by forceps are dangerous to mother and child and that Cesarean section has a high mortality in these cases. If the child is dead or dying, craniotomy is permissible, although this may be difficult. He believes that pubiotomy is the operation of choice where the chin rotates posteriorly and the child is living and in good condition. About twenty years ago, at a time when American obstetricians were doing symphysiotomy, the reviewer had a series of 8 cases of symphysiotomy for disproportion between fetus and mother. In the *Medical News*, a medical journal not now existing, he published a paper in which he advocated symphysiotomy for posterior rotation of the chin in face presentation, and stated his intention to perform the operation should such a case present itself. This did not happen, however, and symphysiotomy was abandoned for other procedures.

The Care of Pregnant Women.—At a meeting of the Section of Obstetrics and Gynecology, Royal Society of Medicine (*British Med. Jour.*, November 11, 1916), a discussion upon this subject was opened by MOORE. He estimated that in England and Wales 3500 deaths occur from childbirth each year. A study of the conditions producing these deaths showed that a very large percentage might be prevented. As a remedy he would advise notification by the patient of her pregnant condition so that she could without fail receive competent medical care. This had actually been tried out in the town in which he lived, a small fee being paid to doctor or midwife for the notification which was only allowed with the consent of the woman herself. In 1536 labors occurring among these patients, 156 of the pregnancies, or 10 per cent., had been notified and received attention during pregnancy; of these, 130 were uncomplicated and 26 required special attention. ROUTH stated that at Queen Charlotte's Hospital in one year 557 cases of albuminuria were admitted. The study of statistics shows that there are 30 per cent. of stillbirths and that it is not at all uncommon to have the birth of a macerated fetus occur. Thus, 25 per cent. of stillbirths show this condition. He believed that care should be given the woman during pregnancy and that postmortem should be made on all stillborn children and search instituted for the characteristic germ of syphilis. BERKELEY described a plan for the establishment of maternity centers which should give supervision of pregnant patients and secure proper care for them and proper attendance during labor. He estimated that 50 per cent. of all pregnant women engaged mid-

wives, and among working women, 75 per cent. BARRETT considered it essential that not only should there be a hospital center, but a local center as well. Much can be done by visitors in the houses of patients who can obtain their confidence. Three activities were necessary: medical, educational and social. The medical needs were three: supervision during pregnancy, attention during labor and supervision during lactation, and for these an obstetric specialist should be available for each mother. On the educational side knowledge concerning healthy pregnancy, delivery and infancy should first be given at a center and afterward repeated in the home of the patient. On the side of social service suitable houses and appliances must be provided for care during parturition. In cases in which no room in a house could be set aside for the use of the parturient woman, hospital conditions were necessary. The pregnant woman should be relieved of the burden of household work in the interests of herself and the child. At the hospital center there should be consultation clinics for maternity cases, infants and children up to school age and prematernity beds and provision for pathological study. MUNRO KERR divided all pregnant women into three groups: (1) Those who were abundantly able to secure good care; (2) a large number of the lower middle class where complications sometimes developed which could usually be cared for without difficulty; (3) the lowest class in the social scale who could not be reached by appeals but who must be governed by legislation. He believed that notification of pregnancy to the patient's physician should be made compulsory and that after the confinement had occurred a report concerning the case should be sent to the medical officer of health. As a penalty for not obeying this law there should be a reduction in the maternity benefit. KRIVSKY, of Petrograd, reported on the conditions in Russia. In European Russia in fifty central provinces there had been a decline in the birth rate from 49.9 per cent. per 1000 in 1894 to 1896 to 43.1 per cent. per 1000 in 1913. The death rate had also lessened from 36.3 per cent. per 1000 in 1892 to 1895 to 27.4 per cent. per 1000 in 1913. The natural increase in the population during this period was 15.7 per cent. per 1000. There was a high mortality among children under one year of age, namely, 27.2 per cent., which was in marked contrast with the same rate in Sweden, 7.1 per cent.; Norway, 6.7 per cent. In 1913 there were 5,249,677 births reported, among which were 870,000 miscarriages and stillbirths. In Russia there were needed for lying-in women 37,000 beds, and to attend the poor, 60,000 midwives instead of the present insufficient number, 14,761. In 1912, 7,033,507 children were born living, and of these 25,240 were born in lying-in hospitals. To show how insufficient is the medical care of this population, 95 per cent. of these confinements were without any obstetrical help whatever. From the stand-point of the midwife PAGET thought that four things were necessary: the early registration of patients, modern teaching for midwives, facilities for medical treatment and the selection of the right sort of person to train as midwives. If compulsory notification were established it would prevent the early registration of these cases. Midwives would do their part in improving the public service if they were given a chance to cooperate with the authorities.

Treatment of Placenta Previa.—HELLIER (*British Med. Jour.*, November 11, 1916) in treatment of placenta previa discussed the field of Cesarean section. He believed that the majority of obstetricians agree that when a patient has had one well-marked hemorrhage that the pregnancy should be terminated without delay. If the patient was not in labor and uninfected and the services of a competent obstetric surgeon could be procured there was much in favor of Cesarean section. He described the case of a patient who had a severe hemorrhage who was treated expectantly, and who died during a second hemorrhage while an attempt was made to perform version. In two other cases he had operated so soon as hemorrhage occurred, with the best results for mother and child. He believed that these patients should be immediately sent to a hospital so soon as a hemorrhage developed. This did not mean that all should be treated by section, for many could be delivered in other ways, but the facilities of a hospital are necessary in the treatment of these cases.

The Morphin-hyoscin Method of Painless Childbirth.—HAULTIN and SWIFT (*British Med. Jour.*, October 14, 1916) published their clinical experience at the Royal Maternity Hospital, Edinburgh. They make no distinction between scopolamin and hyoscin, and use the latter. They had 40 consecutive cases, and while they could not give each a separate room, they darkened the room by placing a screen about the patient and stuffed the patient's ears with cotton to prevent hearing. The first dose given was usually $\frac{1}{4}$ grain morphin, $\frac{1}{150}$ grain hyoscin. Hyoscin alone had no control over pain. In 3 cases only was the morphin repeated. In the remainder the hyoscin was repeated, the average number of injections of hyoscin in each case being eleven to twelve. The greatest number of injections in all was forty-five, which included two doses of morphin. The results were total amnesia and analgesia in 30 out of 40 cases, or 75 per cent. Because the patient could not remember the pain of labor, she asserted that she had no pain when questioned after labor had ceased. There was some effect in all the cases. In 1 case restlessness was so great that the injections were stopped. In 1 case there was postpartum hemorrhage. In 14 cases it was necessary to use forceps, and in 5 of these no chloroform was given. In the other 9 cases when the attempt was made to interfere with the patient, she became restless and it was necessary to use chloroform to apply forceps. There were 5 stillborn children among 40. In one of these cases only had the labor been normal. Among 35 children born living, 4 required artificial stimulation. In using this method the writers think that in a primipara one must wait until the os admits two fingers, and the pains are regular; in a multipara the injection should be given at once. The second injection, $\frac{1}{450}$ grain of hyoscin, is best administered an hour after the first. It is thought that this can be safely repeated at intervals of one hour or three-quarters of an hour afterward. The reader is cautioned not to repeat the morphin in the latter part of the second stage, and that if the hyoscin is not taking effect it is well to give the mother a slight whiff of chloroform so that the hyoscin is allowed to work and the patient goes again into the "twilight sleep." The patient's friends must be kept away absolutely and the room kept quiet and dark.

Patients if thirsty must be given water to drink. The catheter must be used during long labors. The baby must immediately be taken away after birth so that the mother cannot hear its cries, otherwise she will remember the labor. This seems a most extraordinary narration and illustrates the remarkable acumen of the scientific gentlemen who carried out the experiment and the extraordinary credulity of their patients. The percentage of forceps deliveries is that usually seen with or without these drugs, and the writers assert that they use forceps frequently. Nothing is said concerning lacerations, and the percentage of fetal asphyxiation is practically normal. The statement is made that pain is not prevented but that forgetfulness is induced, and that what one does not remember does not hurt. We have long been accustomed to look to Scotland for subtle psychology, and we welcome in obstetric practice this extraordinary contribution to the psychology of parturition. Not having the subtle intellect of the Scot, we fail to recognize its physical value.

Perineal Anesthesia in Labor.—KING (*Surg., Gynec. and Obst.*, November, 1916) reviews the anatomy of the perineal region, and based upon this, has used a 2 per cent. solution of novocain to which is added $\frac{1}{3}$ minim of 1 to 1000 solution adrenalin chlorid to each cubic centimeter. The landmarks are obtained by palpating the pubic arch, and the site of injection is prepared by washing with alcohol or benzine followed by tincture of iodine. The site of each injection is slightly sprayed with ethyl chlorid. The perineal region is divided into two triangles, anterior and posterior, and in the anterior region the needle is entered from 2 to 4 cms. above the lower margin of the vagina, and 2 cms. from the rami. The needle is passed through the fascia, and 1.5 c.c. of the 2 per cent. solution are used for each injection. In the posterior triangle the site of injection is on a line drawn through the anus, and the needle is inclined laterally, entering mid-way between the anus and tuberosities. The injections are made bilaterally. Primiparæ require only the anterior injection, but multiparæ usually need both anterior and posterior. The only unfavorable result seen after this method of treatment consisted in slight superficial necrosis of the inner portion of the labia, but this cleared up without harm. Anesthesia began in a few minutes and was prolonged from two to four hours. Lacerations were diminished in number and extent, and hemorrhage from lacerations greatly diminished. Repair was made much easier because the tissues were not sensitive. The method of sterility employed proved to be practical and satisfactory, and can be readily carried out in private houses.

The Application of Anoci-association to Obstetrics.—HOAG (*Surg., Gynec. and Obst.*, November, 1916) has applied to obstetrics the principle of anoci-association which has received attention in surgery. He combines with this anesthesia by nitrous-oxide oxygen. The objections made to this method have been a lack of muscular relaxation in manipulation, and difficulty in carrying out the principle of local nerve-blocking; 30 cases received perineal injections; 20 were given nitrous oxide; only 4 were given nitrous-oxide and oxygen until the time of delivery, when chloroform or ether was given, and 6 received chloroform in the usual

way. The perineum in all cases was injected with 0.25 per cent. novocain, varying from 60 to 150 c.c. Eleven of the patients received in addition from 30 to 40 c.c. of 1 per cent. quinin-urea solution. In any case the maximum amount of the two solutions injected was 175 c.c. The injection was made as the head appeared in sight; the edges of the vulva were turned back and a long needle inserted at the junction of the skin and mucous membrane, the fingers of one hand being in the vagina to note its position. At this stage of labor the perineal floor is flattened out by the head, but not stretched to any degree. Experience shows that there is no difficulty in infiltrating the levator ani muscles and the perineal body. Novocain was injected first and the quinin-urea immediately afterward. A group of 20 cases were treated by nitrous-oxide oxygen only, and of these 17 received from one to five doses of scopolamin during the first stage before the gas was used. The initial dose was $\frac{1}{200}$ grain with $\frac{1}{6}$ grain morphin or $\frac{1}{2}$ grain narcophin. The scopolamin was repeated during labor. In 4 cases where labor was prolonged a second smaller dose of morphin or narcophin was given. No effort was made to secure the mental condition known as "twilight sleep," because a clear state of the mind is necessary for the successful use of gas. The gas was given before the end of the first stage or at the beginning of the second, according to the distress of the patient and her ability to pay for the gas. The private cases who received this treatment had professional anesthetists, understood exactly what was attempted, and suffered very little. The clinic cases did not do so well. They were not relieved of pain, and with many of them ether or chloroform had to be used. During the actual stage of expulsion complete anesthesia for a few moments was secured. Apparently labor was somewhat shortened by this method, the use of the forceps was no more frequent than with other methods, nor were lacerations more frequent or extensive. In a few cases the injections produced edema and tenderness in the tissues, but no complication developed which interfered with the healing of the lacerations. There seemed to be better dilatation and relaxation of the perineum. In no case could it be proved that the method injured the child. The conclusions of the writer are that the use of small quantities of scopolamin during the first stage of labor is a distinct advantage, shortening the time during which gas is required and giving a much better result. The injection of the perineum seems also desirable. This combined treatment is called by the writer "anociation," and is thought to promise well in obstetric practice.

Combined Tubal and Uterine Pregnancy.—SULLIVAN (*Jour. Am. Med. Assn.*, March 17, 1917) reports the case of a woman in her fourth pregnancy who, while doing housework, had violent pain referred to the diaphragm. This was relieved by morphin, and examination showed the uterus somewhat enlarged, while nothing abnormal was found in the cul-de-sac or abdomen. Two hours later an indistinct mass could be felt in the cul-de-sac. The patient was removed to the hospital and operation performed. In the pelvis and cul-de-sac were clotted blood and a fetus. These were removed, the bleeding tube ligated, drainage inserted, and the abdominal wound closed. By palpating the uterus the outline of a fetus could be felt within its cavity. The patient recovered well from the operation and did not abort. She subsequently gave birth to a vigorous male child.

OPHTHALMOLOGY

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

DENVER, COLORADO,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,

PHILADELPHIA.

Traumatic Sympathetic Ophthalmia.—POULARD (*Ann. d'ocul.*, December, 1917, p. 697) resumes his attacks upon current ideas regarding the danger of sympathetic ophthalmia and preventive treatment of the same by enucleation of the injured eye. He shows the inconveniences which follow enucleation as regards the appearances of the subsequent prosthesis which are always bad and frequently entail grave prejudices to the wearer to the extent even of affecting his means of gaining a livelihood. He would substitute for this operation a partial ablation, the results of which are better from every point of view—mobility, absence of depression at the orbital margin, etc. He believes there is an unwarranted fear as regards sympathetic ophthalmia in the minds of many ophthalmologists. Hence arises the utterly unjustifiable opinion that this is a disease of daily occurrence, an habitual complication of wounds of the eye. As a matter of fact it is at the present time a rare disease; most oculists have never seen a case. He himself, although exposed to meeting it, in that he does not practise preventive enucleation, has seen but a single instance several years ago, and that in the practice of a colleague. He details this case at length in a separate article (*Annal. d'ocul.*, December, 1917, p. 702): An officer was wounded in the eye April 30, 1915; the latter harbored a foreign body. Preventive enucleation was practised forty days after the wound. The other eye remained healthy for four months, when the signs of sympathetic ophthalmia appeared which terminated in total blindness in two months. He presents this deplorable instance to the consideration of both those who do and those who do not believe in the frequency of sympathetic ophthalmia, and emphasizes the appearance of the first symptoms four months after preventive enucleation. In reply to these strictures, Morax, in the same journal, p. 705, tabulates a series of cases of sympathetic disease, from which he draws the conclusion that to be a certain preventive of sympathetic ophthalmia, enucleation must be practised during the two weeks succeeding infection of the ocular globe.

Continuous Prolonged Treatment by Mercury in Grave Forms of Ocular Syphilis.—ABADIE (*Ann. d'ocul.*, December, 1917, p. 734) remarks that notwithstanding the discovery of arsenobenzol the manifestations of syphilis upon the part of the nervous system, particularly of the optic nerve, are much more frequent and severe than formerly and appear to be becoming more so. To what is this due? Certain writers

ascribe it to weakening of resistance of the nervous system, from the strain of modern life. In support of this view, they call attention to the fact that although syphilis is extremely widespread in the Orient, it rarely attacks the nervous system of those apathetic peoples. He is himself inclined to adopt another explanation: syphilis, all are agreed, is becoming more and more widespread, and the successive and rapid passage of the spirochete from one individual to another may serve to increase its virulence, just as Pasteur was able in an identical manner to augment the virulence of the virus of rabies, but whatever be the reason, atrophy of the optic nerve and chorioretinitis of syphilitic origin, the prognosis of which is regarded as most somber, are of daily occurrence. He believes that it would be less so if two factors in the treatment were more thoroughly utilized: (1) the mode of administration of mercury, (2) perseverance and continuity of treatment. As regards the first of these, there is no doubt but that intravenous injections of cyanide of mercury in doses of 1 c.c. are curative of syphilitic manifestations which resist all other methods of administering the drug. As regards the second point, he thinks that the injections should be persevered in until 30, 40, or even more have been given at progressively lengthened intervals. In the great majority of cases, these infections are well supported; so long as this is the case they should be continued. He has treated a considerable number of such cases for the past twenty years, giving the injections as required. Some cannot go longer than three months without treatment, while others remain stationary one, two or three years without the same when lowered visual acuity gives the signal for further injections. No doubt great perseverance is required both on the part of the patient and surgeon; but this has its reward in that it saves from blindness.

Do Moving Pictures Injure the Eyes?—BAHN (*Ann. Ophthalm.*, No. 3, xxvi, 427) comes to the following conclusions in regard to this question, which is frequently put to the ophthalmologist: Moving pictures, under favorable conditions, do not cause as much fatigue as the same period of concentrated reading. When ocular discomfort is complained of there is usually some ocular defect. When there is no such defect at least four sittings of one and one-half hours each per week can be tolerated without discomfort. Under favorable conditions, moving pictures cause increased fatigue, which, if continued, becomes unpleasant and may be harmful, a condition which is greatly increased by prolonged fixed staring at one spot on the picture, a practise which should not be indulged in. A review of the literature records no permanent harm to the eyes from moving pictures. The fact that 10,000,000(?) persons enjoy moving pictures daily, with no definite reports of specific harm or injurious effect, and with but few complaints of slight inconvenience, prove that the moving pictures can have no injurious effects upon the eyes.

Etiology and Treatment of Iritis.—In a discussion upon this subject before the Ophthalmological Section before the Royal Society of Medicine, England (*Arch. Ophthalm.*, November, 1917, p. 572), the president, Mr. W. LANG, in opening, pointed out how desirable it was to arrive at some agreement as to the cause of iritis. In an analysis of 200 cases he

found that the causes and their percentages were as follows: syphilis, 6 per cent.; gonorrhoea, 12 per cent.; tubercle, 11 per cent.; general affections, 8.5 per cent.; other causes, 25.5 per cent.; pyorrhoea, 37 per cent. Hospital figures would probably show a higher proportion for syphilis than 6 per cent., though recent methods of treating that disease would probably place it lowest in the causes. The percentage for gonorrhoea was also probably low, but recent knowledge of that disease, resulting in the treatment of the genito-urinary system, where the gonococcus was so apt to lurk, would largely prevent gonococcal iritis. Relapses seem to be largely due to pyorrhoea. The sexes were equally affected where tubercle was the cause. Tubercular iritis should be treated as tubercle elsewhere plus local measures to subdue inflammation and to prevent closure of the pupil. In 17 of the cases the patient had either gout or diabetes or herpes of the fifth nerve, or influenza, or pneumonia. Ten had a septic surface on the skin or a mucous surface or cavity; 6 had disease of the tonsils, 23 some affection of the alimentary tract and 7 had trouble in the genito-urinary system. In 1 patient the iritis followed a smart blow on the eye and another had iritis as a sequel of sympathetic ophthalmia. In 74 of the 200 patients there was no discoverable cause except pyorrhoea. Removal of the defective teeth or stumps was followed by a rapid clearing up of the iritis. In 22 other cases pyorrhoea existed as a complication of other conditions. Of the 74 cases with pyorrhoea alone the women were twice as numerous as the men. As 28 per cent. of the patients had septic mouths the aid of the dentist would be of great value.

Tension in Normal Eyes before and after Tonsillectomy.—CARR (*Arch. Ophthalm.*, January, 1918, p. 46) has examined 100 cases to determine what effect if any the hemorrhage, anesthetic and shock of tonsillectomy have upon normal intra-ocular tension. A number of cases of iritis with secondary glaucoma had shown a marked and permanent lowering of tension, along with striking improvement in the iritis, within twenty-four hours after removal of abscessed tonsils. No tension changes had occurred in the fellow eye. The connection between the infected tonsils and the eye lesions seemed clear, yet it was thought best to make a control study of tension in normal eyes before and after tonsillectomy. The material comprised 100 cases of tonsillectomy in patients with no history of eye trouble, with ages ranging from fourteen to sixty-seven years. Pus was expressed from the tonsil in practically every case. The tension was taken under holocain with the Schiotz tonometer, first a few hours before and then twenty-four hours after the operation. In 95 per cent. of the cases practically no variation of the tension was noted. The average tension of the 100 cases was $17\frac{1}{4}$ mm., the lowest 10 mm., the highest 26 mm. His conclusion is that tonsillectomy does not have any effect upon normal intra-ocular tension.

Etiology and Pathogenesis of Chalazion.—DEL MONTE (*Ann. d' ocul.*, October, 1917, p. 607) in an extensive study of this subject concludes that since the Meibomian glands possess no intercommunications a microparasite which gains entrance into one only or several is unable to directly affect the others, but when the epithelium is destroyed and the microorganisms have been carried by means of the

lymphatics into the tissue of the tarsus it is in this tissue that they will exercise finally their pathogenic action. There are accordingly two stages in the pathogenesis of chalazion: In the first or initial stage the process is glandular (penetration of the microparasite into the gland, lesion of the epithelium, proliferative reaction of the surrounding tissue). This primary process, once completed, is final and cannot be renewed; it is therefore limited in time and space, restricted in extension and of brief duration. The second stage, that of diffusion, is extraglandular (transportation of the microparasite into the healthy tarsal tissue, lesion of tissue, proliferative reaction and secondary alteration of the Meibomian glands). This stage may continue for a longer or shorter period, depending upon the pathogenic activity and the possibility of diffusion of the parasite. The process which terminates in the formation of a chalazion may be thought of as follows: Hydration, edema and decomposition (Meibomian epithelium in the initial stage and tarsal in the secondary process or stage of diffusion). Proliferative reaction and formation of a granulomatous nodule, of which the remains of decomposed tissue occupy the center. As regards the manner of action of the parasite it may be stated that it produces a primary lesion, that is to say a kind of necrobiosis or toxic hystolysis which is followed by proliferative inflammatory reaction.

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

EMERITUS PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

Injury to the Ear from High Explosives.—WILSON (*Tr. Am. Otol. Soc.*, vol. xiv, Part II) says the ear stands in a different relation to concussion than any other organ of the body. It is a peripheral mechanism fundamentally affected by varying pressures and especially adapted to register and transform minute pressures into nerve impulses. The nerve impulses are carried to the central nervous system to be there interpreted and utilized—not in one long undivided path but along a path broken at numerous junctions or synapses. At these synapses, communications can be established with other physiological systems. The vestibular system is another finely adapted pressure mechanism, designed to register and signal to the central nervous system pressures produced by movements of the head; here also there is not one unbroken path but an interrupted mechanism with many complex associations with other paths. The symptoms associated with loss of hearing from high explosives are varied and complex. There are present, for instance, headache, sleeplessness, lethargy, tremors, vasomotor disturbance, and exaggeration of tendon reflexes. There is unsteady equilibrium with vertigo. There is concentric narrowing of the fields of vision. In many

fields of anesthesia are present. Hyperesthetic areas are occasionally demonstrable. Speaking generally, one may say that we have here symptoms frequently and advantageously grouped under the term "traumatic neurosis." As a result of the high explosive with enormous and sudden increase of pressure in the ear there occurs a dissolution of the permanent auditory pathway and a spread of the nerve impulse into other adjacent paths. The auditory stimulus no longer reaches its goal and deafness results. Such a dissolution may occur at one or several synapses. It may not be complete and a maximal stimulus may still be able to get through. To help the reestablishing of the normal we have the fact that habit and association of activity facilitate transmission of impulses. Nerve impulses tend to pass over an accustomed and long established path, so the most favorable cases are those in which complete dissolution has not occurred. The most unfavorable are those where there has been complete dissolution and total deafness to tuning-fork, voice and noise, no matter the intensity of pitch. The treatment is stimulative of normal function: (1) Tuning-forks are applied at first to the bone; after these are readily perceived, sound is conducted through resonators attached to the ear by a tube and finally through the air. In the worst cases the time given varies with the amount of deafness. Intensity plays little or no part, summation of the stimuli being the effective means. (2) As early as possible the voice is used, at first through resonators with tube in ear, then through speaking tubes and finally without any aid. (3) Each period of treatment is short, for fatigue is rapidly produced. If the treatment is too long there will be headache, vertigo, sweatings and occasionally pain in the ear. (4) As soon as possible carefully graduated physical exercises are given. Here the essentials are short duration and no bending. The treatment (except the drill) is given twice a day in the worst cases, and when it is difficult to pass from bone to resonator the piano is used. At each successive stage there must be summation of the auditory stimuli; thus not only must the fork on the resonator be kept up for some time, but with the voice the word must be repeated, and even then there is often a delay before the response comes, it appearing to be not so much that the patient does not hear, but that he hesitates to attach the word to the sound, for if asked what he thinks it is he frequently answers correctly. In an ear totally deaf to the voice, if the semicircular canals are active, there is justification in continuing treatment for some time. The author concludes that: (1) The normal stimulus (musical notes or voice) is an adequate stimulus for the nerve and is the best stimulus. Electricity is contra-indicated and likely to do harm, since it so easily produces vertigo. (2) In the totally deaf, bone conduction is perceived before air conduction. It is essential to differentiate vibrations from musical notes. (3) In these cases, summation of stimuli plays an important part in the perception of sound. (4) There is a marked diminution of the duration of hearing along the whole series of forks—both through bone and air. This corresponds and exists *pari-passu* with concentric limitation of the fields of vision. Often both improve together. Frequently the field of vision is more retracted on the side having the greater deficiency of hearing. (5) If the conducting mechanism is damaged or destroyed, it not only takes longer to get improvement but complete recovery cannot be expected. (6) Prognosis is good,

as a rule, especially when there is no trauma demonstrable in the peripheral organ, and a normal caloric reaction. The most noteworthy exception met with so far is damage to the seventh nerve. In these cases hearing returns but slowly and so far as we have observed not perfectly, even with a normal drum membrane, little if any signs of middle ear inflammation, and a caloric reaction present.

Radium in Diseases of the Ear.—HARRIS (*Tr. Am. Otol. Soc.*, vol. xiv, Part II) concludes, as a result of an extended investigation, that radium, up to the present time, has failed to be of any considerable benefit in the treatment of diseases of the ear. So far as chronic deafness is concerned it has proved virtually a failure. In the rare cases of intractable tinnitus and excessive vertigo, on the one hand, it can be employed with a reasonable hope of relief by its power of destroying the labyrinth. Finally, so far as malignant growths are concerned, it is of value when they are superficially seated. When deep seated there is nothing sufficiently encouraging to be said of it to warrant its use to the exclusion of operative measures when they can with propriety be adopted. The work that has already been done with it on the ear is not sufficient to condemn it *in toto*, however, and it is to be hoped that other investigators will take it up and give it further thorough and careful trial.

Some Observations on the Bárány Tests as Applied to Aviators.—BABCOCK (*Boston Med. and Surg. Jour.*, December, 1917) sums up the results of more than 1000 observations in the aviation tests for equilibration by means of the American modification of the Bárány chair, and a collaborative determination of the corresponding pulse rate, the summation of the latter, taken in 1000 cases, being as follows: Average pulse rate per minute before turning, 78; average pulse rate per minute after turning, 87; average pulse increase per minute, 9; lowest pulse rate per minute before turning, 58; highest pulse rate per minute before turning, 108; lowest pulse rate per minute after turning, 60; highest pulse rate per minute after turning, 124. In 80 cases the pulse rate increased after turning; in 12 cases there was no change; in 8 cases the pulse was lower after turning; the greatest increase was from 80 to 116, or 36; the greatest decrease was from 76 to 66, or 10; These findings cover a wide range of variation. Taking the general average it can be said that in 100 cases the stimulation to the vestibular portion of the eighth cranial nerve end-organ by fifty revolutions, at varying rates of speed, produced an increase in the rate of heart action of nine beats per minute. Taking the cases separately they may mean little or nothing. The responsiveness of the pulse rate to mental conditions probably accounts for the 8 cases which showed a lower rate after turning, due to the fact that some of the men approached these tests with considerable apprehension. In a very few cases an active reflex with the tenth cranial nerve has caused vomiting, especially after stimulation of the vertical canals. In no case has the candidate fainted, although when it is anticipated he is strapped in the chair.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

Etiology of Granuloma Inguinale.—This lesion, because of its occurrence in the region of the groin and external genitalia, has often been referred to as a venereal granuloma, though recent studies deny this origin. It is endemic in certain tropical and subtropical countries, and is occasionally found in temperate regions. WALKER (*Jour. Med. Res.*, 1918, xxxvii, 427) had an opportunity of studying a number of cases in Brazil. Specimens were obtained for histopathological analysis, and a bacteriological study was also carried out. From the open ulcers a variety of microorganisms could be demonstrated. In the Giemsa smears, spirochetes of different kinds were commonly present. Interesting cell inclusions were observed in the large mononuclear cells. These cell inclusions varied, some of them appearing like vacuoles while others had the character of stained rods. The author believed that the variety of cell inclusions was the result of disintegrative changes of ingested cells and debris. However, some of the materials bore a close resemblance to the intracellular organisms described by Donovan. This type appeared to be encapsulated and the organism varied from oval bodies to distinct rods. The author was able to isolate from a number of cases an organism having the morphological and cultural characters of the bacillus mucosus capsulatus. A number of animal experiments carried out with organisms belonging to this capsulated group of bacteria gave rise to lesions resembling those spontaneously developing in man. It is suggested that the infection in man is gained through abrasions or develops as a secondary infection with other lesions.

Experimental Perforating Wounds of Abdominal Viscera.—The experience gained in previous wars and in civil surgery has demonstrated the vital necessity of early operation in wounds of abdominal viscera. DRUMMOND and FRASER (*Jour. Path. and Bact.*, 1917, xxi, 457) have sought to learn some of the principles underlying the repair of perforating wounds of the abdominal alimentary canal by producing in hares, cats and dogs wounds similar to those caused by bullets. They have been able to corroborate surgical experience of the protective action of the omentum and of plastic peritonitis between the coils of bowel. They found that, following these sudden scissor wounds, the omentum, being perhaps parietic, was not attracted to the injured point, and they put forth the hypothesis that this positive chemiotaxis occurs only when the bowel has been bruised and not perforated, without offering experimental evidence for such migration of omentum in these animals. When the omentum was attached to the wound at operation, vascular anastomosis between it and the gut wall occurred in seven days, except

that when the duodenum and upper jejunum were perforated, omental grafts were of little value. Another protective feature was the plugging action of a small sacculation of the mucous coat through the wall at the site of the puncture. The authors found that single, and occasionally multiple, small wounds of the stomach and bowel may recover and that wounds of the ileum show a greater tendency to spontaneous cure than those of any other part of the intestinal tract.

A Contribution to the Serological Classification of the Bile-soluble Diplococci.—It is somewhat remarkable that a group of streptococci shares with certain protozoa such as trypanosomes, spirochetes and amebæ, the property of readily undergoing complete solution in the presence of bile or bile salts. So far as is known no other bacterial species shows this peculiarity. Other very definite biochemical features mark sharply this group from the other streptococci, and yet in spite of this considerable confusion at present exists in regard to their differentiation. All bacteriologists agree they are pneumococci, but there is no agreement that all pneumococci are bile-soluble and show the other characters attributed to them. Until recently all the bile-soluble diplococci were regarded as belonging to one species, of which the approved name appears to be *Streptococcus lanceolatus*, Gamaléia (1888). Evidence is now accumulating to show that it is necessary to divide the groups into two or more species. MAIR (*Jour. Path. and Bact.*, 1917, xxi, 305) regards the causal infective microbe in scarlet fever as a distinct member of the group. To avoid confusion with Klein's *Streptococcus scarlatinæ* he offers the name of *Diplococcus scarlatinæ*. The only certain criteria at present available for the distinction of the different species and groups of bile-soluble diplococci are serological. Investigating the etiology of scarlet fever, Mair showed that a bile-soluble diplococcus of a special serological type occurs with great constancy in the throats of scarlet fever patients. This diplococcus on subcutaneous injection into monkeys produces a condition which in several respects resembles a scarlet fever in the human subject. In attempting to differentiate the scarlatinal diplococcus by complement-fixation methods from certain closely related bile-soluble diplococci, which occur with considerable frequency in apparently normal throats, difficulties were met with, and for this reason sera prepared from the rabbit and a precipitin reaction was employed. By means of this test four scarlatinal strains were isolated. Of 100 cases it was found that in about 90 per cent. of scarlet fever cases the *Diplococcus scarlatinæ* could be isolated in the first week, and by a set of control tests—normal throats—it was discovered that the frequency of the occurrence of scarlatinal carriers is of the same order as that of diphtheria carriers, and is possibly somewhere near 2 per cent. of the general population. More general application of the method here used may show the relationship of these various strains to one another, and so give more information as to their pathogenic action in the various diseases with which they may be associated.

Formation of Bone in Calcified Epithelioma of the Skin, with Some Remarks on Metaplasia.—NICHOLSON (*Jour. Path. and Bact.*, 1917, xxi, 287) reports a case of neoplasm of the skin which had undergone ossi-

fication. As a tumor it is rare and the process by which the bone arises, whether one of metaplasia or differentiation, is of great interest. Briefly described it was a slowly growing and clinically innocent epithelial neoplasm found in the subcutaneous tissue of the pectoral region of a man, aged forty-one years. It was surrounded by a capsule which, however, was incomplete and through which projected a few processes of epithelium. It was squamous in type, prickle cells and intercellular fibers being present. Evidence of keratinization was found. The whole of the tumor was necrotic. The epithelium was calcified, calcification being most intense at the periphery of the acini. The greater part of the stroma was liquefied and had disappeared. A few of the fibers had calcified. The death of the tumor was due to deficient blood supply, as a few thick-walled vessels were present. At a date subsequent to its death a part of the tumor had invaded from the subcutaneous tissue by granulation tissue. This replaced the old stroma and partially removed the calcified dead epithelium by means of foreign-body giant cells. A narrow zone of uncalcified epithelium was often present in immediate contact with the granulation tissue, where its fibroblasts came in contact with the dead masses they acquired delicate processes and laid down bone with lacunæ, canaliculi, lamellæ and Haversian canals. The bone did not extend any distance into the tumor but was limited to the edges of the epithelium, except where it replaced a small calcified portion of the old stroma. Thus we have a squamous-celled carcinoma of the subcutaneous tissue with its origin in a cutaneous cell rest or graft in embryonic life. As for the changes that occurred in the tumor and that culminated in the appearance of bone, they were of two kinds, regressive (necrosis and calcification) and progressive—the invasion of a part of the tumor by vascular granulation tissue, of decalcification and removal of the epithelium by means of foreign-body giant cells and its replacement by bone. The interesting question to be considered is whether the fibroblasts were converted into bone corpuscles by a process of metaplasia or one of differentiation. The fibroblast, especially when in a state of active proliferation, has very slight differentiation and is not (in appearance at any rate) very far removed from the cells of the mesoblast of the embryo. Now metaplasia is the assumption by one differentiated tissue of the morphological structure and functions of another differentiated tissue. It should be clearly distinguished from the differentiation of embryonic tissues. It is usually found apart from neoplasms in association with irritation, mostly of a chronic nature. As the fibroblast is the cell, which of all those in the body is chiefly concerned with repair, Nicholson sees no reason why with unusual stimuli it should not be able to produce some of the mesoblastic tissues, bone for instance. Metaplasia is a term he believes which should be reserved for a metamorphosis and should not be extended to a simple differentiation.

Immunity by Transplanting Tuberculous Lymph Nodes into Animals.

—The authors of this research, WEBB, RYDER and GILBERT, state (*Am. Rev. of Tuberculosis*, 1918, i, 693) their hypothesis as follows: "If bacilli instead of being injected free into tissues, with no special capacity for resisting or detaining them, were introduced into the substance of a

tissue supposed to have a special defensive function against them, and already in a state of reaction to them, the results might show some diminution of virulence or some increase in immunity in the new host." Guinea-pigs were used in the experiments. The first series of animals were inoculated subcutaneously with 300 bacilli and a month later the inguinal lymph nodes were excised and transplanted subcutaneously into a new series. These animals in turn developed tuberculous lymphadenitis and the inguinal lymph nodes were inoculated into new animals, and so on with succeeding series. The wound of implantation heals in about two weeks, at which time the inoculated tissue is surrounded by a granulation tissue developing from the host. Caseation continues within the node and may ulcerate on the skin surface. From the third to the fifth week the inguinal glands of the host become involved and the animal not uncommonly is overwhelmed with a tuberculous infection as if inoculated by free bacilli. The authors have not been able to determine any increased resistance on the part of the inoculated animals, nor were they able to demonstrate any modification in the virulence of the bacilli. Tuberculin tests are negative until true infection of the tissue of the host has taken place. The implantation of a second tuberculous nodule after the first has been established leads to what appears to be a tuberculin reaction. The difficulty in all these experiments lay in the progressive general infection. In another series of experiments the authors attempted to obviate this difficulty by covering the transplant with a coating of celloidin. The difficulties in these experiments arose from the repeated sloughing of the inoculated mass. In one instance the nodule was retained ten months. This animal showed no evidence of disease, and repeated tuberculin tests were negative. They were able to demonstrate diffusion from within the celloidin coating by transplanting a large tuberculous node beneath the skin of a tuberculous guinea-pig. A reaction developed in the vicinity of this node similar to that from tuberculin.

The Etiology and Pathology of Rocky Mountain Spotted Fever.—WOLBACH (*Jour. Med. Res.*, 1918, xxxvii, 499) has added a third report to his previous preliminary contributions. He had previously described the lesions in guinea-pigs and monkeys. These lesions were essentially those of the vascular system. A microorganism was observed as a minute rod, surrounded by a clear zone and occurring in the endothelial and smooth muscle cells. Similar parasites were found in ticks (*Dermacentor venustus*). From his further studies the author is convinced that the parasite does not belong to the protozoa nor has it the characters of ordinary bacteria. He suggests that it probably represents a new form of microorganism. The author has had an opportunity of carefully studying 3 human cases of Rocky Mountain fever. In 2 of them there was a history of tick bite a few days before the onset of illness. Autopsy examinations were made in 2 cases and in the third skin from various parts of the body was obtained. The important findings were the presence of extensive vascular lesions in the skin and subcutaneous tissues of all parts of the body. The vessels in the deep corium and fat are often thrombosed. The earliest lesion is a collection of endothelial cells over a swollen portion of the intima. The elastic

fibers are fragmented. The minute parasite is found in these endothelial cells and in the muscle fibers of the media. Similar lesions are present in the veins. It is noteworthy that the bloodvessels of internal organs do not show this reaction.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,
WASHINGTON, D. C.

Scarlet Fever during 1915 in Philadelphia.—OSTHEIMER (*Am. Jour. Pub. Health*, October, 1916, vol. vi to x) states that during 1915, 1072 cases of scarlet fever were reported in Philadelphia, exactly 100 more than half the number reported in 1914. There is a morbidity rate of 63.7 per 100,000 as compared with 117 in 1914 and 208 in 1913. The lowest number of cases was reported during August, 29 cases; the highest number during December, 147 cases. As to the sex of the 1072 cases, 529 were males, of which 513 were boys and 543 females, of which 501 were girls. These figures are the lowest since 1900, as is also the death-rate from scarlet fever during 1915, which is only 26 in the entire city; 74.6 per cent. of the cases were reported to the Bureau of Health within three days from their onset. Girard College furnished the only institutional epidemic of 31 mild cases, and there were also two small school epidemics of 12 and 10 cases each. No cases were traced to milk infection. Statistics of the number of cases in the different wards and districts were made and it was found that the density of population had no relation to the number of cases. When the primary case was treated at home, 117 secondary cases occurred later than twenty-four hours, but within one month after the first case; but only 31 secondary cases occurred when the primary case was removed to the hospital for treatment. During the year of 1915, 625 cases, or 58.3 per cent., were removed to the Philadelphia Hospital for Contagious Diseases, while 447 cases, or 41.7 per cent., were treated at home. The hospital death rate during the year was 21 deaths, or 3.3 per cent., and the death rate among those treated at home was 5 deaths, or 1.1 per cent.

The Germicidal Effect of Gastric Juice.—GREGERSEN (*Zentralbl. Bakt.*, 1916, Part I, p. 353) found that the bactericidal effect depends wholly upon the presence of free hydrochloric acid. The experiments were carried on with *Staphylococcus pyogenes aureus*. The bacterial emulsion was incubated with 4 c.c. of gastric juice at body temperature.

In the absence of free hydrochloric acid but in the presence of hydrochloric acid combined with amino groups there is a very slight germicidal effect. The presence of even small quantities of free hydrochloric acid results in a very material increase of the germicidal power, compared to which the effect of the combined hydrochloric acid is insignificant. The effect is in proportion to the quantity of free hydrochloric acid present. It has been found that the free acid present in the gastric juice resulting from Ewald's test breakfast was four times as effective as an equal quantity of free acid in an artificially prepared solution. This is explained by the presence of certain substances in the dry toast which by themselves are not germicidal. These extractives are capable of raising the germicidal power of the free acid present. Pepsin has been found to be of no influence.

A Modification of Roemer's Intracutaneous Method for the Determination of Small Amounts of Diphtheria Antitoxin in Blood Sera.—ZINGER (*Jour. Infect. Dis.*, October, 1916, No. 4, vol. xix) describes a convenient, practical and economical test for the determination of the antitoxin content of blood. The test is important in dealing with many experimental and clinical problems connected with the subject of diphtheria. The advantages of such a test are that: (1) The L + dose of the toxin is taken as the test dose and so diluted that each cubic centimeter represents $\frac{1}{100}$ L + dose. (2) Two test points are established with each serum, the test at which no lesion develops, and the one for twice the amount of antitoxin at which a distinct lesion appears; within these two limits lies the antitoxin content of the serum. (3) It saves animals because 4 tests can be made on one guinea-pig. (4) As little as $\frac{1}{200}$ unit of antitoxin can be determined in a serum with a fair degree of accuracy. The details of the test are as follows: (1) A standard, well-ripened toxin is used, so diluted with normal salt solution that 1 c.c. represents $\frac{1}{100}$ L + dose. (2) The serum to be tested is used either undiluted or diluted 1 to 10, 1 to 100, etc. The amount of serum used in the test is always 0.2 c.c. except when the test is made for $\frac{1}{200}$ unit of antitoxin, then 0.4 c.c. is used undiluted and is added to 0.2 c.c. of toxin solution. (3) Normal salt is used to balance the mixture. (4) After putting together the toxin, serum, and salt solution the mixture is allowed to stand for thirty minutes at room temperature before injection into the guinea-pig. (5) Four injections are made in each pig, the abdomen being divided into four quadrants and the injections made as far apart as possible. (6) The places of injection are examined at the end of 24, 48, 72, and 96 hours and the results noted, *i. e.*, whether and to what degree there is redness, induration, or necrosis. In the interpretation of results, the absence of lesion at the site of injection indicates that the serum on test has completely neutralized the toxin solution and contains therefore more than the unit of antitoxin tested for; the presence of necrosis indicates that it contains less than the unit of antitoxin while the presence of a lesion indicates that it contains the unit of antitoxin.

The Control of Communicable Diseases in Schools.—BAKER (*Am. Jour. Pub. Health*, October, 1916, No. 10, vol. vi) states that in time past the school has been accused of being a focus for the dissemination

of infection and the occurrence of the "contagious diseases of childhood" is associated with the beginning of school attendance. But the school with its segregation of the children also offers a great opportunity for early detection of cases of communicable disease. The prevention of communicable diseases by the exclusion from school of children showing any symptoms of such diseases is a very important part of the system of medical inspection of schools. In order that such a system may be effective, the child should be excluded from attendance and isolated before he has a chance to infect others. In New York City the system has been worked out as follows: Each school receives a printed list of all cases of communicable diseases reported to the Department of Health on the previous day. This list is sent to every teacher and the name of each pupil who is entered on the list or who is a member of the patient's family is noted. Such children are excluded from school at once. The names are reported to the school nurse who reports each day to the school inspector. When two or more cases of any disease have occurred in any one class-room, the inspector examines each child in that class-room every morning and excludes suspicious cases. Each school is visited by the school doctor or school nurse each day and every child who shows any evidence of illness is examined by them as well as those returning after illness or an unexplained absence. At this time, any child who shows any symptoms indicating a communicable disease is excluded. Additional preventive measures included in this scheme are a monthly routine inspection of all children in each school and physical examinations with consequent follow-up visits to adjust unsanitary and unhygienic home conditions. During the six years that this system has been in effect, it has not been necessary to close any public school in New York City on account of an epidemic of communicable diseases and out of an average school population of 800,000 children in New York City, an average of five thousand or less than 1 per cent. have been necessarily excluded each year because of the presence of a general constitutional disease. The author concludes with the statement that such medical control of schools may be exercised in any community and the school instead of being the focus for disseminating disease may become a very valuable means of checking the spread of communicable diseases.

Experimental Cholera Carriers.—SCHÖBL in a previous communication showed the relative values of various methods to make cholera carriers of guinea-pigs. The duration of the state of parasitism following intravesicular inoculation, the distribution of cholera vibrios throughout the alimentary canal, and the elimination of cholera vibrios in the feces of the experimental cholera carriers were studied. SCHÖBL (*Jour. Infect. Dis.*, August, 1916, xix, No. 2) now reports further studies along these lines and comes to the following conclusions: Sufficient evidence has been gathered, it is believed, to justify the opinion that the condition in question is an infection of the gall-bladder, and that the cholera vibrios injected into and recovered by culture from the gall-bladder stand in causal connection with the pathological changes encountered, instead of merely surviving as saprophytes at the place of inoculation. The infectious process may vary in extent and intensity, remain limited to the gall-bladder or extend to the liver. The absence

of cholera vibrios from blood from the lungs and from the spleen makes the septicemic character of the infection highly improbable. With regard to the intravesicular inoculation the rabbit's behavior differed from that of the guinea-pig, inasmuch as the inflammatory process which followed the injection of cholera vibrios brought about the occlusion of the gall-bladder, so that the cholera vibrios were no longer to be found in the intestine at a time when they were still present in the contents of the gall-bladder. It is evidently a benign process which shows marked tendency to healing, *i. e.*, the cholera vibrios disappear from the animal's body and the animal survives, although a large percentage of the animals showed signs of chronic intoxication.

The Value of Cholera Immunization.—KONRÁDI (*Zentrabl. Bakt.*, 1916, Part I, p. 339) states that following vaccination the blood will show agglutination for about a year. The protection conferred by vaccination depends upon the number of inoculations, the dosage, and upon the mode of living. An annual dose of 0.5 c.c. is sufficient. The vaccination is free from danger even to children. The author employs Kolle's method of preparation of cholera vaccine. The bacterial emulsion is heated for one hour at 55° C. One-half per cent. phenol is added. One c.c. of the emulsion contains 2 mg. of culture. The first dose is 0.5 c.c. An additional 1 c.c. is injected after one week. The symptoms are slight and usually disappear within two days. The author's experience is based upon 1400 immunizations.

The Incidence of Pellagra in Spartanburg County, S. C., and the Relation of the Initial Attack to Race, Sex and Age.—SILVER, GARRISON and McNEAL (*Arch. Int. Med.*, August 15, 1916, xviii No. 2) give as their purpose "the presenting of recorded facts in respect to incidence of pellagra and its death rate in the year of initial attacks in each year since the appearance of the earliest recognized case in the county and the correlations between race, sex and age on the one hand and incidence of pellagra and death rate in initial attack on the other, as shown by the total cases on the records at the end of the field work in 1914." The paper deals only with initial attacks and not with recurrences of the disease. The authors studied first the incidence of pellagra in each year, and found that the number of recognized cases in the county had increased progressively each year since 1907, more rapidly up to 1911 and at a less rapid rate up to 1914. As to the death rate in the year of initial attack, they found it to be 15.8 per cent. for the 1180 recorded cases. The death rate was higher up to 1911 but there was no decided indication of a progressive change in it after that time. As the result of their study of the important relation of race, sex and age to pellagra the authors have reached the following conclusions. The death rate in initial attack has been 41.8 per cent. for negroes and 12 per cent. for the white race. It was found that the disease has more severely attacked the white race than the negroes of the county, but that in late years there has been a slow but progressive increase in the ratio of negro pellagrins to white pellagrins. Pellagra has rarely been found under the age of one year, but is not so rare in the second year, and during the period from two to twelve years it is quite common. The death rate in initial attack has been low in

children. In cases of infantile pellagra, evidence of close residence with another pellagrino is usually early noted. The milk of pellagrino mothers is not considered by the authors to be the cause or the vehicle of the cause of pellagra in infants. The period from twelve to sixteen years is relatively free from initial attacks of pellagra. After sixteen years, the incidence of pellagra rises rapidly in women, especially in colored women, among whom the death rate has been 46.7 per cent. in the year of onset during the period from sixteen to twenty years. Between the ages of twenty and fifty years the number of women pellagrinos gradually decreases. The number of men attacked gradually increases during this period so that at fifty years the two sexes are about equal. The onset of pellagra in old age has been found to be somewhat more common in men. In white women over twenty years of age the death rate has been found to be 11.9 per cent., increasing progressively from 4.6 per cent. in the third decade to 47.6 per cent. in the seventh decade of life. For analogous groups of white men, colored women and colored men the death rate has been 21.2 per cent., 40.2 per cent., and 50 per cent., respectively, increasing slightly with age in all these groups. A table recording the incidence of pellagra per 10,000 population in respect to race, sex, and age gives the following computations: Incidence per 10,000 for white male population, 231; incidence per 10,000 for colored female population, 81; incidence per 10,000 for colored male population, 25. In the age period ten to fourteen years, the incidence is low in all groups. In white female population it is highest in the age period thirty to thirty-four years, namely, 535 per 10,000. In white male population it is 325 per 10,000 in the period from fifty-five to fifty-nine years. In colored female population it is 241 per 10,000 in the period from thirty to thirty-four, while in colored males it is 33 per 10,000 in the period from sixty to sixty-four years. Another table shows the proportion of initial attacks in children under twelve years of age to be increasing. In 1910 they were only 3.7 per cent. of the total recorded cases, while in 1914 they were found to be 29.7 per cent. of the total recorded cases. In the opinion of these investigators the relatively lower incidence of pellagra among the negroes of Spartanburg County is due to the fact that they are, in a large measure, segregated from white pellagrinos and that the disease is not so persistently present among them because they die much more rapidly than do white pellagrinos, due to greater poverty and poorer diet. The study of racial and age differences in the incidence of pellagra show that poverty and poor diet are important factors in determining the death rate among pellagrinos but that they are important only in connection with close association with antecedent pellagrinos if the original onset of the disease is under consideration.

Different Types of Streptococci and Their Relation to Bovine Mastitis.—MATHERS (*Jour. Infect. Dis.*, August, 1916, No. 2, xix) finds that hemolytic streptococci of human origin produce mastitis in cows, as Davis and Capps have shown, when injected directly into the milk ducts. This mastitis may be severe, leading to a caked bag and later to a chronic inflammatory condition which results in an atrophy of the mammary gland. On the other hand, virulent hemolytic streptococci may grow and multiply in the milk ducts of a cow without causing

any visible changes in the udder. The milk, however, as these observations show, contains hemolytic streptococci and an increased number of leukocytes. These infections may persist over long periods of time in the form of a chronic mastitis. *Streptococcus lacticus* of the type used in these experiments produces a very acute inflammation of the udder when cultures are injected directly into the milk ducts. This infection in my experiments was of short duration and left the gland functionally unchanged. A non-pathogenic hemolytic streptococcus of the type commonly found in normal milk may give rise to a transitory inflammation of the udder when injected directly into the milk ducts, producing a mastitis similar in every detail to that produced by non-hemolytic *Streptococcus lacticus*. The presence of pathogenic streptococci and an increased number of leukocytes in milk is indicative of a mastitis, and may be the sole indication of mastitis. The quarters of a cow's udder under experimental conditions are apparently separate as regards infection. One quarter may be infected while the others remain normal. Examination of the milk from each quarter of the udder is necessary before mastitis can be excluded in a suspected cow. In three instances of bovine mastitis, all of which were due to hemolytic streptococci with all the characteristics of the human types, no noteworthy changes in the morphology or cultural characteristics of the invading organisms were observed in frequent examinations of the milk throughout the course of the infections. The distinguishing characteristics primarily noted for each organism were still present at the last observation, and there were no modifications which might be considered as indicating a change from one type to the other. The cultural and morphological characters of *Streptococcus lacticus* and of the hemolytic streptococcus derived from normal milk did not change during the course of the udder infections which they induced.

Rocky Mountain Spotted Fever in California.—CUMMING (*Jour. Infect. Dis.*, November, 1917, p. 509) states that the results of animal inoculations definitely establish the occurrence of Rocky Mountain spotted fever in California. The finding of *Dermacentor venustus* in Ventura County and the occurrence of a case there marks that region as a new area of possible prevalence of the disease in California. Advantage should be taken of the inoculation test to establish definitely the nature of the seasonal eruptive fever which occurs in Modoc and Lassen counties.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

AUGUST, 1918

ORIGINAL ARTICLES

RECENT DEVELOPMENTS IN INTESTINAL BACTERIOLOGY.

BY ARTHUR ISAAC KENDALL, S.B., PH.D., DR.P.H.,

PROFESSOR OF BACTERIOLOGY, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL;
DIRECTOR OF THE PATTEN RESEARCH FOUNDATION.

THE privilege of addressing the Pathological Society of Philadelphia is one I esteem very highly. The subject suggested for this evening's discourse, "Intestinal Bacteriology," brings into apposition two wide fields of bacteriology which have interested my colleagues and myself for many years, namely, the chemical activities of bacteria, on the one hand, and the nature of the relations existing between alterations in the diet and the character of bacterial response in the alimentary canal, on the other hand.

INTRODUCTION. The belief that the intestinal flora is fundamentally a physiological unit rather than a heterogeneous collection of adventitious microbes has afforded opportunity for a new avenue of approach to this complex subject. Viewed from this angle, the kaleidoscopic aggregation of microorganisms which comprise the normal intestinal flora stands in a rather definite relation to the diet of the host. That is to say, as the diet is changed along definite lines a dual bacterial response may be elicited. The types of bacteria may, and frequently do, shift. Those organisms which cannot accommodate themselves to the new nutritive environment tend to diminish in numbers, and other, more adaptable, types take their place. A less spectacular but frequently more significant response is that in which the products of the metabolic activity of the intestinal microbe change is parallel with the nutritional stimulus. The

metabolic products of normal intestinal bacteria are essentially innocuous, but it is by no means an exaggeration to state that a given bacterium may be potentially either a veritable Dr. Jekyll or Mr. Hyde through the products it forms from one or another normal constituents of the diet of the host. Fortunately the latter organisms are relatively uncommon and abnormal. Many pathogenic bacteria are of this type, however, and their dual chemical personality will be commented upon in an appropriate place.

Information relating to bacterial development in the intestinal tract is derived from two principal sources—the bacteriological examination of intestinal contents at varying levels under varying conditions and artificial cultivation of the same, or similar microbes, singly or in mixtures, attempting to reproduce meanwhile the intestinal environment. Up to the present time it has not been possible to produce an artificial intestinal canal with its complex associated conditions. This of course limits very decidedly the range of experimental possibilities, but the timely utilization of fistulæ in man, intensive studies of animals and other possibilities that suggest themselves are fruitful sources of information. The results which have flowed from experiments and studies on record at the present time, immature though they may be, are full of promise that a new and wide field of therapeutics may be unfolded in the future. For the present a brief summary of existing information and an equally brief indication of the relation of existing theories to future developments must suffice.

ANALYSES OF INTESTINAL CONTENTS. It has been estimated that a normal adult on an average, well-balanced ration excretes daily in the feces nearly thirty trillion of bacteria. The nitrogen contained in the dried bodies of these organisms equals about 50 per cent. of the total nitrogen of the feces, and these dried bacteria alone would weigh nearly 8 gm. More than 0.5 gm. of nitrogen therefore is contained in that moiety of the feces which is composed of bacteria. It is apparent that the food ingested does not contain this very large number of microbes, hence the assumption must be that the alimentary canal is the site of a tremendous daily bacterial proliferation. The alimentary canal is probably the most efficient combined culture medium and incubator known to bacteriology. Striking as these analytical figures may be there is an even more noteworthy phenomenon discernible—that peculiar, well-defined alternation of bacterial types which normally follows very closely the nutritional history of the individual from early infancy to adult life.

INTESTINAL BACTERIOLOGY. At birth the intestinal tract and intestinal contents are normally sterile. The first indications of bacterial contamination are recognizable several hours postpartum. The early invaders are adventitious microbes, similar in every respect to those commonly present in the infant's environment. They gain

entrance to the alimentary canal through the mouth, although the possibility of rectal infection must be borne in mind. As a rule the proliferation of these organisms is limited, partly because the intestinal contents at this time are inadequate to support a large bacterial population, partly because a majority of the bacteria are unable to accommodate themselves to gastro-intestinal conditions.

About the third day postpartum the alimentary canal of the infant becomes permeated with breast milk in place of the colostrum, and this condition prevails in nurslings for several months. A marked change is discernible in the intestinal flora at this time. The heterogeneous, irregularly staining initial microbes disappear to a remarkable degree, and, coincidentally, large numbers of long, slender, Gram-staining bacilli appear. Many of these exhibit slightly attenuated ends. A majority of these belong to the group of *Bacillus bifidus*, and they usually persist in dominant numbers during the nursing period.

The reaction of the feces now becomes definitely acid, indicating a unification in the character of the products arising from the development of the characteristic nursing flora. The conditions just described as characteristic for normal nurslings persist relatively unchanged until the dietary requirements of the child exceed the possibilities of nutrition at the breast alone. It is worthy of note that artificially nourished infants frequently fail to exhibit this rapid homogenation of the intestinal flora; indeed, the flora of infants nourished upon cows' milk or other unnatural food is relatively heterogeneous in respect to bacterial types, as a rule.

As the diet becomes more varied a marked change is noticeable in the general appearance of the intestinal organisms. That monotony of type which is associated with the monotony of diet (breast milk) gives way to considerable variations in size, form and tinctorial reaction of the microbes comprising the intestinal flora. These changes are, generally speaking, a substitution of Gram-negatively staining bacteria of the colon type for a considerable proportion of the Gram-positively staining organisms so distinctive of the flora of the normal nursing, as well as the appearance of large bacilli (many of them spore-forming) cocci and variable numbers of microbes that vary from time to time and from individual to individual.

The consistency and chemical composition of the feces likewise undergo changes which follow the dietary history of the child rather closely. The homogeneous, pasty, acid stool characteristic of nurslings gradually becomes less acid in reaction, somewhat disagreeable in odor (due to the presence of aromatic bodies, such as indol and skatol) and more formed. This change in intestinal bacteria, intestinal contents and in the general character of the composition of the intestinal residuum, which appears to have its origin in the amplification of diet of the young child, progresses

slowly until a new period of stability is reached. This is the time of late adolescence and maturity. The intestinal enzymes are now mature, the dietary habits are well-established and in health the intestinal flora appears to reach an equilibrium. At this time the coliform organisms, few in number in the nursling, comprise more than 50 per cent. of all viable intestinal microbes. It may be stated that coliform bacteria are as characteristic of the intestinal flora of adults as the long, thin Gram-staining bacilli (*Bacillus bifidus*) are characteristic of the intestinal flora of nurslings.

That portion of the above presentation which relates solely to the dominance of *Bacillus bifidus* in the intestinal flora of the normal nursling and its gradual replacement of coliform and other bacteria in older children has been recorded independently by many investigators. It may be confidently stated that it represents accurately the sum total of generally accepted knowledge of this subject at the present time.

The all-important problem for solution is, "Why should there be this striking and fairly definite sequence in the types of bacteria in the intestinal tract, coinciding in point of time with alterations in the diet of the host?" A discussion of this problem together with certain considerations which flow naturally from it form the basis of this lecture. A considerable proportion of the investigations upon which the discussion hinges represents published and unpublished studies of the writer and his colleagues. Naturally, time does not permit of specific mention of them.

A large variety of bacteria certainly gain access to the alimentary canal; of these, surprisingly few types seem to establish themselves. A professional fasting man who has partaken of no food for thirty days, harbored large numbers of colon bacilli in the large intestine, showing very plainly that the accumulated detritus is sufficient to sustain a numerous bacterial population. Normally, many types of organisms are introduced with the food, but of these relatively few appear to find intestinal conditions favorable for their continued growth. Those that do persist are not, as a rule, dominant in the food. Nevertheless, food plays an important part both in determining the types of bacteria which become implanted in the alimentary canal and in regulating the character of the products of metabolism of these organisms incidental to their growth.

The normal diet of the nursling is breast milk which contains nearly 7 per cent. of lactose and but 1.5 per cent. protein. The relatively frequent feedings assures the presence of at least minimal amounts of it in the large intestine at all times. The intestinal flora which is associated with this monotonous diet is conspicuously homogeneous in type and in chemical activity. The dominant organism *Bacillus bifidus* greatly outnumbers all other bacteria and the lactic acid it produces from the fermentation of the lactose gives a physiological acidity to normal nursling feces. There is therefore

a noteworthy parallelism between the monotonous diet of the nursling, the monotony of the bacterial flora in the nursling rectal contents and a continued acid reaction in the nursling dejecta. Artificially nourished infants do not, as a rule, exhibit this phenomenon in its entirety.

These essential details are reproducible in certain laboratory animals. Consequently the general premise that a definite relationship exists between the diet of the normal nursling and the character of the intestinal bacterial flora may be regarded as tentatively sound.

As the child becomes older and the diet becomes more complex the intestinal flora undergoes a distinct change. The significant dietary factor is a material reduction in the proportion of carbohydrate to protein; the striking bacterial response is a sharp decline in the proportion of obligately fermentative bacteria, prominent among which is *Bacillus bifidus*, and a remarkable increase in the coliform organisms, which thrive equally in a medium relatively rich in carbohydrate or in one in which carbohydrate is practically absent. It should be remembered that the dominance of coliform organisms in the alimentary tract does not result from a dominance of coliform organisms in the food. Indeed, the members of this group of bacteria are not particularly numerous in proportion to the other types of bacteria in the carefully prepared pabulum of childhood. In other words, the types of bacteria found in the alimentary canal do not reflect in type or proportion those commonly found in the food.

In addition to the ascendancy of coliform organisms at this period in the digestive history of the child there is discernible a rather well-marked regional distribution of bacterial types from the higher to the lower levels of the intestine. Also, those organisms in actual contact with the intestinal wall do not necessarily coincide in type or numerical distribution with those found at the same level which are in the actual intestinal contents.

An explanation of the phenomena so briefly outlined above clearly involves the dual conception of bacterial adaptation to environmental conditions and the character of their metabolism as well.

Bacteria, from the view-point of alimentology, may be considered as digestive systems working within a digestive system, each individual bacterium being a complete system in itself, the entire viable bacterial population growing within the alimentary canal of the host. There is an important difference between the two systems in that the entire digestive history of the microbe is carried out within the limits of the alimentary canal, whereas only the preparation and assimilation of food for the host occurs within this restricted field. It follows that the products resulting from the intracellular utilization of food by bacteria are excreted again into the intestinal tract, whereas the products resulting from the intracellular utili-

zation of assimilated food of the host do not necessarily reappear in the tract again. The products of metabolism of the parasite, in other words, may react upon the host, but under ordinary conditions those of the host are of minimal consequence to the parasite.

It is probable that the essential phenomena of metabolism of host and microbe alike possess some characteristics in common. The nutrition and general metabolism of bacteria, however, is a subject of recent investigation and not well known. It is pertinent, therefore, to mention briefly certain salient features of it in this connection.

BACTERIAL METABOLISM. Generally speaking, there may be recognized two distinct phases in the life history of a bacterial cell: (1) a structural or anabolic phase, comprising the phenomena of growth and maintenance of the organism and its appendages, including the replacement of losses due to enzyme formation and other vital repairs, (2) and a catabolic vegetative or energy phase which comprises the phenomena attendant upon the energy requirements necessary to maintain the vegetative activities of the cell.

Bacteria are very small. Five hundred million typhoid bacilli would weigh rather less than a milligram. It is apparent, therefore, that even with a very liberal allowance for waste the actual amount of material required to build such a bacterial cell would be very little indeed. Nevertheless, many kinds of bacteria, in spite of their minute size, produce very noticeable and rapid chemical changes in their environment, as a result of their development. This marked disproportion between the size of bacteria and the magnitude of their chemical activity appears to be explainable upon that biological principle which maintains that the energy requirement of living things varies with the surface area rather than the volume of the organism. The volume (and consequently the weight) of a million typhoid bacilli, for example, is extremely small. The aggregate surface, however, is surprisingly large. A million typhoid bacilli weigh approximately 0.002 milligram. The surface area of these bacteria, however, is nearly 10 square millimeters. It is not wholly surprising, therefore, that microorganisms, even as small as bacteria, produce chemical changes in their environment quite out of proportion to their size.

The relation between surface area, volume and the magnitude of the organism's metabolism cannot be carried too far, however. A typhoid bacillus and a proteus bacillus, for example, are very nearly equal in all dimensions; yet a proteus bacillus will induce changes in its nutritive environment many fold greater than a typhoid bacillus. As a general rule, strictly pathogenic bacteria are noticeably less active chemically than parasite organisms, and the latter are frequently much less reactive chemically than saprophytic microbes.

Returning once more to the structural requirements of bacteria,

it is a fact that nitrogen in appropriate combination with carbon, hydrogen and oxygen is absolutely essential for the growth of bacteria. It is not surprising, therefore, that bacteria will not develop in pure saccharine solutions.

The energy requirements, on the other hand, are essentially transformations of suitable combinations of carbon with oxygen and hydrogen. Nitrogen plays an insignificant part, as a rule, in this phase of bacterial activity. When utilizable carbohydrates are present in the nutritive environment of most bacteria the products formed are chiefly those arising from the fermentation of such substances, and chemical evidences of the utilization of nitrogenous substances are minimal.

When utilizable carbohydrates (or similar available non-nitrogenous substances) are not available the bacteria must obtain not only the structural requirements, but the energy requirements as well, from the nitrogenous constituents of the medium. Under these conditions, nitrogenous waste products become relatively prominent. Without entering into details a few well-known examples of the relation between the utilization of nitrogenous and non-nitrogenous substances for energy may be introduced. The diphtheria bacillus, grown in appropriate nitrogenous media containing no utilizable sugar or an amount of sugar which the organism can use up without inhibiting its further activity, will produce a very potent soluble toxin. If the *same* organism is grown in the *same* nitrogenous medium, to which is added sufficient utilizable sugar so that the organism cannot use it up, it will be found that no toxin whatever will appear in the culture. Similarly, the colon bacillus grown in sugar-free nitrogenous media will produce indol, ammonia, hydrogen sulphide and other products indicative of the break-down of protein; but the *same* organism grown in the *same* nitrogenous medium, to which utilizable sugars are added, will not contain any of these products indicative of protein break-down. On the contrary the characteristic products are organic acids, carbon dioxide and hydrogen.

The proteus bacillus is one of a considerable number of bacteria which produce a soluble enzyme in sugar-free gelatin, which liquefies this protein. The sterile filtrate of such a liquefied gelatin culture will contain enough free enzyme to liquefy an additional amount of gelatin. The addition of a *small* amount of utilizable sugar to gelatin cultures of the proteus bacillus will prevent *temporarily* the formation of this enzyme in an active state and the addition of a *considerable* amount will *permanently* prevent the development of the gelatin-liquefying enzyme. It is worthy of note that the mature, soluble, gelatin-liquefying enzyme, freed from bacteria by filtration through a porcelain filter, will liquefy sterile gelatin containing the same sugar which *in culture* prevented the formation of the enzyme, clearly suggesting that the presence of utilizable carbohydrate

prevented the *elaboration* of the enzyme, but had no effect upon the *action* of the enzyme once it was excreted in an active state.

The relation between the factors which form the production of this proteolytic enzyme and those which are associated with its action when it is mature is even more striking. Chemical examination of cultures (free from utilizable carbohydrate) in which the enzyme develops in increasing proportions shows the presence of increasing amounts of ammonia. A similar examination of sterile gelatin mixtures (with or without carbohydrate), in which the germ-free enzyme induces liquefaction, fails to reveal any increase whatsoever in ammonia. Apparently the activity of the enzyme is independent of ammonia formation. Nevertheless, ammonia formation invariably occurs when the enzyme is formed by the bacillus. The facts presented would seem to justify the following deductions: The soluble, gelatin-liquefying enzyme of *Bacillus proteus* is formed when the organism utilizes protein for its energy. It is not formed in an active state when utilizable carbohydrates are *continually* available for energy. (Small amounts of carbohydrate insufficient to prevent the development of the organism have been shown in similar experiments to inhibit enzyme formation until the carbohydrate is used up. Acid within the limits of tolerance of the organism does not inhibit enzyme formation.) The function of the enzyme is to prepare protein for assimilation by the organism, as the enzymes of the alimentary canal of man prepare proteins for assimilation. Ammonia formation is a measure of the deamination of the assimilated protein fragment and not a concomitant feature of the action of the enzyme *per se*. The ammonia is "bacterial urea." Other organisms which form similar soluble proteolytic enzymes react in like manner to the presence of utilizable carbohydrates.

The protective or sparing action which utilizable carbohydrate exhibits for protein or protein derivatives in cultures of bacteria has its counterpart in higher organisms. The underlying principle is apparently analogous to that in man: Physiologists have long stated that the oxidation of carbohydrates protects the protein of the body. Carbohydrates, in other words, are protein spacers, and, as Howell has aptly stated it, "as the carbohydrate food is increased the protein food may be diminished down to a certain irreducible minimum, which is probably the amount necessary for the reconstruction of new tissue." The sparing action of carbohydrate for protein of bacteria is chiefly of significance in relation to the energy phase of bacterial metabolism.

It might be claimed that the toxicity of the protoplasm of bacteria would be a factor to be considered in this connection. Space does not permit of a discussion of the diminution of nitrogen in the bodies of bacteria developed in saccharine solutions as contrasted to that of the same organisms grown in nitrogenous media of otherwise similar compositions.

The sparing action of utilizable carbohydrate for protein in cultures of bacteria has a deeper significance than has been realized hitherto. The diphtheria, colon and proteus bacilli, to mention merely those referred to above, form widely different products as the result of their growth in nitrogenous media from which utilizable carbohydrates are excluded. The same is equally true for typhoid, paratyphoid, dysentery, hemorrhagic septicemic, tetanus, "gas," symptomatic anthrax and many other pathogenic bacilli, cholera and other vibrios and a large number of saprophytic organisms as well. Stated differently, it is positively known that diphtheria and tetanus bacilli form highly specific soluble toxins as they develop in protein media. They form innocuous fermentation products, chiefly acids, as lactic and acetic, from the same media to which utilizable carbohydrates are added. That which makes diphtheria and tetanus bacilli formidable, in other words, is apparently inseparably associated with their growth in nitrogenous but carbohydrate-free media. The antithesis of this specificity of products developed in nitrogenous, sugar-free media is manifested in the remarkable similarity of products formed in the same media which contains utilizable carbohydrate in addition. The nitrogenous products formed by typhoid, dysentery, cholera and other pathogenic organisms are unknown as yet, but the simple addition of utilizable carbohydrate to cultural media in which they are grown causes them to produce fermentation products, as lactic acid, precisely as the diphtheria bacillus does under similar circumstances. The chemical products formed by these bacteria in the presence of utilizable carbohydrate are potentially those produced by the Bulgarian bacillus; that is to say, a large number of bacteria pathogenic for man become potentially lactic acid bacilli when they are grown in fermentation media, and from this point of view, therefore, their specificity of action is inseparably associated with the utilization of protein for energy.

Typhoid, dysentery and diphtheria bacilli do not ferment lactose. If milk contained dextrose in place of lactose, or if at least 0.5 per cent. of dextrose were added to it, these organisms would produce sour milk as the result of their growth in it and this sour milk would not differ qualitatively from that produced by the Bulgarian bacillus. Furthermore, so long as the bacteria were confronted with this dextrose they would continue to make sour milk until the acidity reached a degree incompatible with their further growth. If the utilizable carbohydrate were removed, of course they would act once more upon the protein.

CORRELATION BETWEEN THE DIET OF THE HOST AND THE TYPES OF BACTERIAL FLORA IN THE INTESTINAL TRACT. Turning now to the alternation which takes place in the bacterial flora of the intestinal tract from earliest infancy to adult life, it has already been stated that the change in the intestinal bacteria follows very closely

the change in the diet of the individual. During the nursing stage, when the diet is almost wholly breast milk, the bacteria discernible in the intestinal contents and, when proper methods are used, cultivatable from the intestinal contents, are very largely of a single type known as *Bacillus bifidus*. *Bacillus bifidus* is an obligately anaërobie organism whose chemical activity is restricted quite closely to the fermentation of milk-sugar and other carbohydrates resulting in the formation of lactic acid.

In the absence of lactose this organism grows very poorly, and this is quite in accord with the well-known disappearance of *Bacillus bifidus* when the diet of the young child is relatively restricted in carbohydrates with a coincident increase of the protein. Lactose is present in breast milk to the extent of 7 per cent., while the protein is less than 2 per cent.; therefore the milk-sugar, under normal conditions, permeates the entire intestinal tract of the nursing. It is not surprising, consequently, to find that an organism which utilizes lactose readily without producing products inimical to the well-being of the host is one which is prominently represented in the nursing intestinal flora. It has been actually possible in a considerable number of experiments (particularly those carried out in young animals) to reproduce the characteristic nursing flora, with a very considerable amount of faithfulness by suitable feeding experiments. Similar experiments carried out in older animals are frequently unsuccessful, however, an explanation for this difference in response not being available at the present time.

When the diet of the child becomes more varied, which usually means a coincident diminution of the proportion of carbohydrates to protein, the normal, homogeneous intestinal flora gives way to a more heterogeneous picture, in which, however, there may be recognized at least a well-defined tendency for certain types of bacteria to thrive at particular levels in the intestinal tract. It is of course obvious that at any given level there will be found, in addition to those bacteria which find conditions favorable for their development, representatives from higher levels as well. The latter organisms are presumably transported mechanically with the intestinal contents to the lower levels. Consequently, the fecal flora contains representatives of all the microbes which develop freely in the intestinal contents. It should be remembered, however, that the large majority of the fecal bacteria are either weakened in vitality through the accumulation of waste products, the effect of desiccation and other factors, or they are dead.

It should be repeated that one of the most important factors which plays a part in bringing about this change in the intestinal flora is the carbohydrate content of the diet, particularly the relative reduction in the proportion of lactose. Carbohydrates, generally speaking, are readily hydrolyzed into hexoses, and as readily absorbed from the alimentary tract. Proteins, on the other hand,

undergo a comparatively elaborate simplification before assimilation. It follows, therefore, that the natural result of a reduction of carbohydrate in the diet and the relatively rapid assimilation of carbohydrate from the intestinal contents is the establishment of a zone in the intestinal tract where under normal conditions the amount of carbohydrate waxes and wanes. At this level it might be confidently predicted that *Bacillus bifidus* would not thrive, because, as has been stated previously, this organism is almost obligately dependent upon carbohydrate, and particularly upon lactose, for its rapid development. It might be reasonably assumed therefore that at a level where there would be alternate periods of carbohydrate and lack of carbohydrate there would be found bacteria whose metabolism would be equally well maintained in a medium in which carbohydrate would be present one time and absent later. Such an organism is indeed found commonly in the intestinal tract under these conditions, and it is represented to the extent of nearly 60 per cent. in the viable fecal flora. This organism is *Bacillus coli* and it grows rapidly in media containing carbohydrate and almost equally rapidly in media containing no carbohydrate. Time does not permit of an extension of the discussion along these lines because there are certain other aspects of gastro-intestinal bacteria which must be at least briefly mentioned.

BACTERIAL IMPLANTATION IN THE INTESTINAL TRACT. Somewhat more than a decade ago, Metchnikoff published that very interesting but somewhat speculative book called *The Prolongation of Life*, in which he called attention to a possible parallelism between premature senility, that very indefinite condition spoken of as auto-intoxication and the possibility of microbial stagnation, leading to the overgrowth of bacteria which produced substances acting as cumulative poisons. To combat these somewhat hypothetical toxicogenic bacteria he proposed to infect the intestinal tract with lactic acid bacilli. Although many of the assumption on which this theory was based have not yet received confirmation, the concrete idea of bacterial implantation within the intestinal canal for therapeutic purposes opened a new and interesting field for study.

Very briefly the theoretical procedure was to introduce into the alimentary canal living cultures of suitable organisms which would colonize and through the formation of certain products—benign to the host but inimical to the bad microbes—restrict the activity of the latter or even drive them out. The organism selected for this purpose was *Bacillus bulgaricus*.

Observations made by different observers upon experimental animals have shown almost conclusively, however, that the *Bacillus bulgaricus* does not acclimatize itself readily in the large intestine, where the microbial cesspool is most active. If published observations are correct, *Bacillus bulgaricus* is an organism which for scores of years has been cultivated in milk outside of the human

body. It requires a great deal of courage to predict that an organism which has been cultivated exclusively outside of the body in milk for many years should be able all at once to adapt itself to intestinal conditions, and it is not surprising to find that the implantation of *Bacillus bulgaricus* has left much to be desired.

There is, however, an organism, or, more properly, a group of organisms, relatively common inhabitants of the lower intestinal tract of man, which possesses the requisite qualifications for development within the alimentary canal, and inasmuch as they are normal inhabitants of the region where colonization is desirable, these bacteria would appear to be the logical candidates for this type of therapeutics.

In order to be certain, however, that *Bacillus acidophilus* (for that is the name of the organism) will colonize successfully and certainly within the intestinal tract the mistake must not be made of keeping cultures of this organism too long upon artificial media before introduction into the body. That is to say, the artificial perpetuation of a strain of *Bacillus acidophilus* for long periods of time outside the human body may so modify its adaptability to intestinal conditions that it will not fulfil the purpose for which it is intended. Fresh isolations from the intestinal contents should be made as frequently as is necessary to ensure active acclimatizing strain. Failure to realize the importance of these relatively simple and perfectly obvious details has prevented the accumulation of a satisfactory literature upon the highly important practical aspects of bacterial implantation.

In addition to the obvious necessity of securing a suitable microbe for intestinal bacterial therapeutics it is equally essential to provide the proper food for the organism. The food for the organism is naturally that portion of the intestinal contents flowing through the section in which the microbes are growing. If the object of intestinal implantation is to restrict the putrefaction of protein derivatives—and this is usually the object sought for—it is perfectly obvious that a decided reduction in protein in the diet is an important initial step. The next step is to increase the carbohydrate of the diet, but it is imperative to ascertain if the carbohydrate in utilizable form actually reaches the desired area. If, for example, the reduction in protein and increase in carbohydrate is assured, but there exists a sluggish motility in the higher layers of the alimentary canal, the inevitable tendency is for the rather rapidly assimilated carbohydrates to be absorbed, leaving a residuum of protein derivatives, which are naturally hydrolyzed more slowly. Under these conditions, although the diet may appear adequate and correctly proportioned on the diet sheet, it may well happen that the amount of carbohydrate actually reaching the lower intestinal tract is so limited that the desired object of a continued supply of utilizable sugar is not realized. Enough has been said to suggest at least

the nature of the factors which must carefully be considered before accepting or rejecting the efficiency of bacterial implantation.

There are contra-indications to bacterial implantation and these may be theoretically of at least two classes. If the condition to be corrected is one which is associated with a relative intolerance for carbohydrates (and such conditions are not uncommon, although they are frequently not recognized), then clearly the administration of carbohydrate as such is not likely to be productive of the best results. On the other hand, there are occasional diarrheal conditions in the intestinal tract which are associated with, even if not caused by, an overgrowth of bacteria which are able to ferment large amounts of certain types of carbohydrate in an abnormal manner in a very short time. Some of these microbes, even in an artificial medium, may actually use up 5 per cent. or more of sugar within a period of a comparatively few hours: How much more active may these organisms be in the intestinal tract, where, generally speaking, conditions for their development may be much more favorable than in artificial cultivation! Experience has shown that under these two conditions, namely, where there exists an intolerance of carbohydrates and where there may be present an unusual number of fermentative bacteria in an active or latent state, which would act energetically upon a sudden increase in the carbohydrate in food, the best results are obtained by administering sour milk. Apparently, although proof is still lacking upon this point, the considerable amount of preformed lactic acid in well-soured milk spreads rapidly through the intestinal tract, because of the increased peristalsis which is usually a factor of such cases, and brings about chemical improvement, which may be rapid or slow, depending upon conditions. The organisms which exhibit unusual intestinal fermentative activity are, so far as is known at the present time, intolerant of lactic acid.

From what has been said it must be obvious that in theory at least there is a very close relationship between the diet of the host and the nature, extent and type of bacterial development which takes place within the alimentary canal. When the diet is monotonously rich in carbohydrate, so that the entire tract is permeated, as it were, continuously with sugars, the natural tendency is toward a great increase of bacteria whose fermentative activities are prominent. The products of growth of these organisms are not inimical to the host, as a rule. This is shown by the great preponderance of *Bacillus bifidus* in the normal nursing and the ability to encourage to a marked degree an aciduric flora in suitable experimental animals by carefully conducted feedings. When the diet of the host is so modified that there is no longer a preponderance of carbohydrate throughout the intestinal tract, then there becomes manifest a regional strata of microbes whose metabolism is accommodated to the ordinary fluctuations in diet. In those levels in which carbo-

hydrate is not continuously present and from which it occasionally disappears, it is not surprising to find that bacteria which accommodate themselves with almost equal readiness to media, with or without carbohydrates, become prominent. This is shown by the remarkable increase in colon bacilli in the intestinal contents of adolescents and adults. From the ileocecal valve onward the presence of carbohydrates is usually irregular and the colon bacillus consequently thrives better because of its adaptability in this respect than does *Bacillus bifidus*.

BROMATOLOGY AND BROMATHERAPY. Certain theoretical therapeutic applications present themselves if the above observations are correct. Hundreds of experiments in artificial media have shown that the typhoid bacillus, dysentery bacillus and many other pathogenic bacteria produce substances akin to those characteristic of sour milk, when they are grown in the presence of utilizable carbohydrate, and products undoubtedly associated with the decomposition of proteins when carbohydrate is absent. In the case of the diphtheria bacillus the cultures in utilizable carbohydrate contain no toxin, whereas those cultivated under parallel conditions in media without carbohydrate produced considerable amounts of very potent toxin. Would it not be logical, in intestinal infections, as, for example, in dysentery or cholera, to attempt at least to flood the intestinal tract with considerable amounts of suitable carbohydrates and thereby provide the necessary non-nitrogenous pabulum for these organisms? Unless conditions within the intestinal tract are fundamentally unlike those in artificial media (an improbable supposition because the carbohydrate under discussion is a distinct chemical entity), it is reasonable to expect that some of the nitrogenous products formed by these bacteria may then be replaced by lactic acid and similar non-toxic fermentative substances; in other words, create dietary conditions within the alimentary canal potentially like those of a normal nursling and confidently hope for an analogous bacterial response. Of course the damage which may have resulted from the growth of pathogenic bacteria prior to the change in diet cannot be undone, but there remains the strong theoretical possibility of reducing, or even preventing, additional harm through this shifting of the metabolism of the invader by the utilization of carbohydrates for energy, with the resultant formation of definitely benign products.

It must be emphasized in passing that an occasional aberrant fermentative flora be not aroused to unusual activity by this change in diet. Fortunately, such cases are relatively uncommon and readily controlled if they are recognized when the change is made.

The researches of Coleman upon diet in typhoid fever have indicated that the high calorie diet, relatively rich in carbohydrate, does exert an influence upon the patient which is not fully explained on the assumption of sparing the nitrogenous loss of the body, due to

the fever and toxemia. The reduction in toxemia which is frequently observed will be explained in part at least by an absorption of carbohydrates from the intestinal tract, providing thus not only in the intestinal tract but in the tissues and blood as well a maximum amount of utilizable sugar. The tissues of the body are not called upon to furnish their own fuel. The normal blood contains not far from 0.08 per cent. of dextrose. A large carbohydrate intake would tend to keep the glycogen reservoir in the liver and possibly other organs at a high physiological level. The relatively small amount of dextrose used by the bacteria within the tissues would thus constantly be replaced. Coincidentally, the reduction of putrefaction and the accumulation of lactic acid formed not only by the pathogenic bacteria, but by normal intestinal microbes as well, would tend to lessen rather than to increase irritation from bacterial products formed within the alimentary tract. Coleman and his associates have actually found that the beneficial effects of feeding on this high calorie diet were rather more marked in those individuals whose intestinal tracts contained active members of the aciduric group, and they have reached the conclusion that an artificial implantation of *Bacillus acidophilus* may well be an important adjunct in the high calorie dietary treatment of this disease. The intestinal group of diseases, typhoid, dysentery, paratyphoid and cholera, would all appear to be amenable to this form of bromotherapy.

An hypothesis or theory developed in a growing subject which does not suggest more than it answers is a poor one indeed. In conclusion, therefore, a theoretical extension of the intra-intestinal aspects of bacterial metabolism, bacterial implantation and bromotherapy to abdominal, intestinal and rectal surgery may legitimately be considered. It is a matter of rather common observation that perforating wounds of the upper intestinal tract are, on the whole, less dangerous to the patient than similar lesions lower down. Various explanations have been advanced to explain this phenomenon, and emphasis has been placed upon the comparative paucity of microbes in the duodenum and upper stretches of the intestines. This is apparently true during interdigestive periods. There is, however, a rapid rise in the number of bacteria when food enters the upper levels which would indicate that the kinds of organisms or their activities might be of some importance as well.

From the view-point of alimentology it is an assured fact that carbohydrate will normally be present in the duodenal sector as the food passes through, and it is not surprising to find that the duodenal flora is, on the whole, relatively carbophilic. The theoretical possibility of inducing a similar condition throughout the tract is in the realm of possibility, as is clearly shown in that great natural experiment in the nursling's alimentary canal. The two important factors to be considered in inducing an appropriate intestinal flora

as a preoperative measure are, diet and, in the lower intestine, bacterial implantation. It should be possible to assist the dietary factor materially in those instances in which carbohydrates in appropriate amounts do not reach the desired level by rectal administration, and this process readily admits of a simultaneous implantation of bacteria to assure a nucleus of desirable microbes upon which to build. Such a procedure can do no harm and the possibilities are decidedly in favor of the patient. If this is successfully carried out the dangers from intestinal infection should be materially lowered, a point of some theoretical importance to the surgeon.

SUMMARY. 1. There appears to be an intimate relationship between the character of the diet and the nature of the intestinal flora.

2. This relationship, bacterially considered, is manifested by an adaptive intestinal acclimatization of fairly definite types of bacteria. Changes in the diet, if prolonged, tend to change the types of bacteria. A change in the products of metabolism of intestinal bacteria is also induced, depending upon the presence or absence of carbohydrate. Positive implantation of adventitious microbes—those not accommodative to intestinal conditions—appears to be infrequent.

3. Bacteria which are normally acclimatized do not produce metabolic products widely at variance with the well-being of the host. Toxic or irritating metabolic products tend to arouse the antagonism of the host. The results may be disease, expulsion of the microbe, immunity or the carrier state.

4. Products arising from the utilization of food for energy by intestinal bacteria are of paramount importance in determining the specificity of action of these microbes. To a limited degree a careful modification of the diet may materially alter the character of these metabolic products, with benefit to the host. Bromotherapy may be practised in acute or chronic disease.

5. Bacterial implantation within the alimentary canal must follow natural lines. Bacterial acclimatization and adaptation is the resultant of complex reciprocal activities between host and parasite.

6. Intelligent bacterial implantation presupposes an accurate knowledge of the chemistry of the metabolic products of the bacteria under varying dietary conditions.

7. It is unwise to generalize from incomplete data. The data of bromatology and bromotherapy in relation to microbial activity in the alimentary canal are conspicuously incomplete. Nevertheless, the remarkable influence of diet upon the activities of intestinal bacteria, in so far as it is known, would warrant the assumption that a new chapter in the broad field of bacteriology has just opened. The indications are apparently favorable for a new avenue of approach to bacteriotherapy.

THE FREQUENCY OF PROTOZOIC ENTEROCOLITIS IN THE MIDDLE WEST: CLINICAL MANIFESTATIONS, DIAG- NOSIS AND TREATMENT.¹

BY FRANK SMITHIES, M.D., F.A.C.P.,

CHICAGO, ILL.

ASSOCIATE PROFESSOR OF MEDICINE, COLLEGE OF MEDICINE, UNIVERSITY OF ILLINOIS;
GASTRO-ENTEROLOGIST TO AUGUSTANA HOSPITAL; FORMERLY GASTRO-
ENTEROLOGIST TO MAYO CLINIC, ROCHESTER, MINNESOTA.

(From the Division of Diseases of the Digestive System, Augustana Hospital.)

STUDY of the records of the last 1000 stool analyses in my clinic at Augustana Hospital indicates that therein 93 instances protozoa were observed. Inasmuch as the patients furnishing these specimens were largely from the northern half of the middle west—a region where man is commonly considered to be free from protozoic infection—it would seem not altogether valueless to review this material from its clinical aspects. Apart from those in tropical countries, but little mention of such findings exists in medical text-books. Vague, archaic descriptions of the parasites together with illustrations common to laboratory manuals for decades have been firmly engrafted on the mind, medical, throughout the country—and this in spite of the emphatic and complete articles by Darling, Craig, Deeks, Freund, Sistrunk, Lyons and Giffin. It would seem quite possible that the local and general increases in population and the ease with which people get from place to place is worth emphasis. The free intercourse between Mexico, South America, the Islands of the Far East and the Southern States of this country may be a not-to-be-neglected factor in a wider spreading of protozoic intestinal infections than has heretofore been recognized.

A. ETIOLOGICAL FACTORS OF THE GROUP. *Age.* The patients' ages ranged from seven years to eighty-two years. The average age was thirty-nine.

TABLE I.—CASES OF PROTOZOIC ENTEROCOLITIS IN THREE YEARS.

Patients with intermittent or chronic diarrhea	86
Patients without diarrhea	7
	93
Patients from south of Springfield, Ill.	4
Patients who had visited in the South	11
Patients who had never been in the South	78
Patients from small towns, rural communities or farms	70
City or large town dwellers	23
Patients who had habitually drunken well or shallow river water	78
Patients whose water supply was seemingly good	15
Patients who were large eaters of fresh garden truck, bananas or unwashed fresh fruits	66

¹ Read before the Chicago Society of Internal Medicine.

Sex. There were 51 males and 42 females. There was practically no difference noted in the sex-age figure.

Nativity. Fifty-two patients were of Scandinavian birth or extraction. The remainder were Americans, Germans, Irish, Russians, Austrians or English.

Geographic Distribution. During the past ten years we have had strongly impressed upon us the importance of gaining information when taking histories, regarding both the present and past residences of patients and also the exact environmental conditions under which they have lived. These points appear to have special significance in the examination of individuals affected with obscure abdominal ailments, particularly when such are associated with diarrhea.

The geographical diversity of patients forming this group was as follows: Illinois 29, Iowa, 16, Wisconsin 13, Nebraska 8, Michigan 7, Minnesota 6, Indiana 4, South Dakota 2, Arkansas 2, Ohio 2, Texas 2, Kentucky 1, North California 1. (Table I.)

It will be noted that but 4 patients came from regions south of Illinois. There were 11 patients who had made occasional business or pleasure trips to the Southern States. There were 78 individuals who had never been south of Illinois.

Water Supply, etc. We routinely seek information not only with respect to the patient's present drinking-water, but also regarding his drinking-water from childhood. The importance of water supply as a source of protozoic infection has been abundantly commented upon in the literature; clinically, we have gained valuable facts from seeking information about it. Not rarely patients admit that for years their drinking-water has been bad, especially such patients as have taken up residence in recently opened "homestead" territory. Shallow, dug wells, contaminated springs, sluggish, weed-grown rivers or ponds or lakes befouled by drainage systems have proved to be the source of water supply in 78 instances. In the remaining 15 cases the drinking-water was seemingly good.

The contamination of garden vegetables by dung is not unlikely responsible for protozoic spread. It is well known that hogs, cattle, sheep, barnyard fowls or snails, worms and flies are common carriers of flagellate protozoa and ameba in their intestinal canals. Instances in which cholera-form epidemics have existed on stock farms are not unknown to veterinarians. It is the usual practice to "fertilize" fields or boxes with "rich" manure in which head lettuce, radishes, tomatoes, mushrooms, celery, etc., are grown. One cannot deny that those who partake largely of these vegetables, raw and often carelessly washed, are in danger of ingesting both active and spore forms of protozoa. Of late years truck farming has become an important industry about every big city—hence the army of "manure-eaters" is not located wholly in the country. City folk who are financially able to afford the luxury of fresh

garden truck may be contaminated during the entire year. The common house-fly not infrequently contaminates fruits, particularly the banana. This fact is well known to Mexican planters who have cleared areas previously endemic with amebic dysentery, by the simple procedure of screening the banana sheds and covering dung mounds with antiseptics, sand or oil. It is quite possible that the prevalence of protozoa in the mouths of individuals in both tropical and temperate countries is due to food and water contamination. These parasites live in filth; if the filth is supplied in the mouth by eroding gums and decaying, dirty teeth (as in pyorrhea) the parasites may thrive and do harm. Soggy tonsils, cancerous, syphilitic, phagedenic or tuberculous ulcers likewise furnish an ideal camping-ground for these unwelcome guests. If the hydrochloric acid of the stomach did not inhibit or destroy these parasites it is not unlikely that intestinal infection would be more universal. What controlling effects digestive enzymes, bile salts or intestinal flora have on these organisms is not known. The mechanical activity of the stomach, duodenum and jejunum may prevent lodgment and multiplication in these parts of the gut, while the stagnation and increased bacterial proliferation of the terminal ileum and of the large bowel may furnish from time to time the proper habitat for protozoic lodgment and growth. That protozoa may exist for a long time without causing symptoms is evidenced by Willets' report that 85 per cent. of all Philipinos habitually harbor these parasites and that but intermittently (spring and summer) do they enormously multiply and produce local and systemic effects.

Of our 93 cases, 66 patients were consistent eaters of fresh garden truck, unwashed fresh raw fruits or bananas.

B. CLINICAL SYMPTOMATOLOGY.

TABLE II.—DIARRHEA PATIENTS.

Duration.	
Less than one year	8
Between one and three years	27
Between three and five years	31
Between five and ten years	12
More than ten years	8
Total cases	86
Attacks of diarrhea—Least number 3 in all	
Maximum number 9 yearly	
Diarrhea, chronic and continuous (summary of 72 cases) . . . 14 cases	

1. *Diarrhea.* In our series this was a presenting complaint in 86 cases. Diarrheic stools without frequent evacuations were not rarely passed chronically, with periods when the movements were frequent. *The intermittency of frequent diarrheic stools, with apparently normal motions in the intervals is quite characteristic of this affection* and aids in differentiating it from the diarrheic stools asso-

ciated with gastric or pancreatic achylia, imperfect liver function, tuberculous or luetic ulceration of the bowel and the like in which ailments the *constancy* of the soft or fluid stools is a common observation. In the event of the diarrheas associated with protozoa, the patient may note no change in his habit, mode of life or diet, but quite suddenly may experience frequent evacuations of the bowels. Occasionally a period of severe mental or physical overstrain or an attack of la grippe, tonsillitis or the like are stated as preceding the diarrhea. The attacks may be infrequent or may come close together over a period of many years. The latter event may supervene upon the former. In our series one patient had had but three attacks, while another case had experienced nine in one year. There were 14 patients in whom the diarrhea had been continuous.

The duration of the diarrhea varies greatly. (See Table II.) Sixty-seven per cent. of our cases had been affected from one to five years; 8 cases had been ill less than one year, while a like number had been ailing for more than ten years; the longest period being forty-three years.

TABLE III.—SUMMARY OF CLINICAL SIGNS AND SYMPTOMS.

(Figures Stand for Number of Cases.)

Clinical observation.	Parasite.					
	Ameba.	Cercomonas.	Trichomonas.	Lamblia.	Megastoma.	Balan-tidium.
Diarrhea	24	33	20	5	2	2
Constipation	1	2	0	0	0	0
Normal stools	2	1	0	0	0	0
Abdominal pain	21	30	17	4	2	1
Dyspepsia	15	28	21	5	1	2
Weight loss	17	30	21	3	2	2
Achylia gastrica	13	12	11	2	1	1
Subnormal acid	8	14	8	2	0	1
Normal gastric acid	6	10	2	1	1	0
Anemia	26	31	18	4	2	2
Eosinophilia (above 3 per cent.)	19	27	15	2	1	1
Blood in stools	14	17	16	3	2	2
Fever	4	1	2	0	0	0
Chill	2	3	2	1	0	1

In character the diarrhea is commonly of the gassy type, without discomfort upon the passage of the stool. Occasionally an associated inflammatory change in the colon, especially in the sigmoid or rectal sections, results in painful evacuations. Hemorrhoids were present in 38 per cent. of our cases. They may become extremely annoying when the motions are very frequent and watery.

The bowel movements are generally easy, but prolonged diarrhea may lead to marked tenesmus and prostration.

Constipation occurred in 4 of our cases, in fact, the most toxic patient appeared for the relief of an obstinate intestinal stasis. Routine examination of the freshly passed stool following saline catharsis disclosed enormous numbers of entamebæ in the histolytica stage and actively motile cercomonads.

2. *Dyspepsia*. This was a prominent complaint in 75 cases (75 per cent.). The dyspepsia was generally associated with nausea (particularly in the morning), eructations of foul gas, regurgitation of sour-food mixtures (even when the stomach analyses revealed absent or low gastric acid), gassy distention of the abdomen, soreness after eating, loss of appetite and occasionally vomiting.

3. *Abdominal Pain or Discomfort*. Abdominal pain or discomfort was a complaint in 89 instances (95.6 per cent.). The discomfort was variously described as colicky (like gas pains following abdominal exploration), soreness, distention, cramp-like, "dragging" or vague "weak feelings." Sometimes the rapid peristaltic movements of the small gut were productive of an annoying discomfort even though actual pain were absent.

4. *Weight Loss*. This was noted in 75 cases (80 per cent.). The loss varied from 5 pounds to 104 pounds. The average loss was 17.3 pounds. Some weight losses were so striking and so rapid as to bring the patient under observation for suspected, atypically located malignancy: a young woman affected with entamebæ and cercomonads lost 104 pounds in less than one year; a middle-aged woman lost 80 pounds in less than fifteen months; a man, aged eighty-two years lost 65 pounds in less than ten months. With the exception of the first case these patients nearly doubled their weights during the year following treatment. The first-mentioned female gained 28 pounds within three months of her discharge from the hospital.

5. *Strength Loss*. Strength loss is often striking even though the weight may have decreased comparatively little. Apart from the possible toxic effect of the protozoic infection, loss of sleep due to diarrhea, imperfect assimilation or diminished quantity of ingested food, continuous abdominal discomfort, anemia and the dread of the existence of an incurable ailment seem to be important factors in the production of a general, systemic weakness.

6. *Anemia*. Anemia is usually evident even though in some cases it may not be pronounced. It is sometimes of a grave degree: certain patients are sent in as pernicious anemia cases or as atypical anemias of unknown etiology.

7. *Mental Attitude*. A peculiar malaise of melancholia is frequently observed. It may be due to a dread of impending evil, continuous headaches (especially common in some instances), weakness, anemia, loss of sleep, abdominal distress or toxic substances occurring as a consequence of the bowel upset.

C. PHYSICAL EXAMINATION.

The patients generally appear both starved and toxic; in this respect the individuals past middle age closely resemble those with malignant disease. The skin often exhibits a dusky, sallow pallor. It is not rarely dry and wrinkled. Subcutaneous fat is lost quite early, although not so early as in malignant disease. There is liable to be edema about the ankles in the severe cases. The visible mucosæ are generally pale, dry and scaly. The saliva is often scant and tenacious. The tongue is usually swollen, marked by the teeth and heavily coated. The breath is heavy and often foul. Focal infections about the nasal passages, teeth and tonsils are not uncommon, but such are not characteristic for this affection.

Thoracic examination often discloses shallow respirations of increased rate, and when weight and strength loss have been rapid such are associated with anemia, signs of lung edema. The heart rate may be slowed, but upon exertion it increases out of reasonable proportion to the amount of exercise. Murmurs, generally systolic, are not uncommon in such cases.

Abdominal inspection revealed visible peristalsis over the small bowels in 22 of our patients (23 per cent.). The waves were often strikingly visible and of very rapid rate. In several instances peristalsis was seen only following sharp tapping of the belly wall with the fingers. Patients had sometimes felt the actively moving small gut and were under the impression that snakes, tape-worms, etc., had developed within them.

Palpation usually made out both small and large bowels filled with gas and feces. This was a common observation in the diarrhea cases. Distention of the terminal ileum was frequently pronounced—the coils felt as large as loops of normal colon.

Tenderness over the small and large gut was noted in 64 cases (69 per cent.). In severe diarrhea it was often marked. Tender areas over the gall-bladder or appendix zones was present in 83 instances (88 per cent.). The liver was enlarged and tender in 3 patients. The spleen was palpable 9 times: in 4 there was definite enlargement.

Rectal Examination. The frequency of hemorrhoids has already been commented upon.

Proctoscopic examinations were made in the last 37 cases coming under observation. Bleeding ulcers were noted in the sigmoid or upper rectum 9 times. In 21 cases a diffuse, catarrhal or granular inflammation of the gut was seemingly of greater grade than the frequent bowel evacuations alone would explain. In these cases the bowel was easily traumatized and in some instances the bleeding following instrumentation was rather severe.

D. LABORATORY EXAMINATIONS.

1. *Stools.* For the detection of protozoa it is absolutely essential that the stool be properly collected. Our procedure is as follows:

Any medicines which the patient may have been taking are stopped. He is then placed upon a liquid diet for thirty-six hours. At the expiration of this period he comes to the clinic. He is given 1 ounce of Epsom salt or 500 c.c. solution of citrate of magnesia upon an empty stomach. The first stool passed is discarded; the second or subsequent stools are collected in a warmed container, mixed with one-fourth volume of warm normal saline solution and examined at once, by high power, in thin smears placed upon warmed glass slides on the hot stage of a microscope. None of the ready-made warm stages are satisfactory. After trying all forms we have come back to the copper plate heated by a Bunsen microburner placed upon the ordinary microscope stage. If such is not at hand an old-time carbon electric bulb placed beneath the microscope stage after the Abbe condenser has been swung to one side answers very well. In suspected cases examination is made of at least six slides before negative opinion is given. Very often examinations are made daily for even as long as a week when the history is suggestive. Frequent examinations of different stools often not only detects parasites that might have been missed but leads to the discovery of multiple infections. High power should be used in the examinations, particularly for entamebæ, because the differentiation of the types may rest upon careful study of cellular architecture. Stained specimens are best prepared by the Hastings-Giemsa method suggested by Darling.²

2. *Macroscopic Examination of Stools.* The stools are commonly of a greenish-brown or yellow color and of a purée-like consistency, intermixed with flakes of mucus and food bits. They may be blood-streaked or foamy. The *reaction* is usually definitely alkaline. The odor is often quite characteristic: a peculiarly penetrating, pungent mustiness that sometimes is definitely ammoniacal. When there is much blood or necrotic tissue the foul, acrid, putrid odor is disgustingly nauseating.

² Fresh coverslip preparations containing a sufficient number of entamebæ to warrant staining and study, or those intended for diagnosis, are made into smears by sliding off the cover slip and thoroughly drying both slip and slide, after which each is stained with Hastings's stain for fifteen minutes. Satisfactory films are then overstained with Giemsa's stain until the film has a diffuse reddish purple tint. The film is then plunged into 60 per cent. ethyl alcohol containing about 1 per cent. of water of ammonia (10 per cent.), and differentiated in this, washed in water, and controlled by the microscope until the purple substance of the nucleus and the blue color of the cytoplasm are strongly contrasted. The film when properly differentiated has a blue-violet color. If the film has been greatly overstained, it is treated with a momentary douche of 95 per cent. alcohol. Beautiful pictures are obtained in this way, but, what is of more importance, the various figures displayed by the purple staining substance (karyosome?) can be noted and followed with ease. This purple staining substance, in the nucleus of *Entameba tetragena* in dried-fixed films, represents only a portion of the nucleus, as the centriole and peripheral chromatin do not stain purple by the above method. The purple staining substance in the nucleus of *Entameba tetragena* frequently appears as a ring, or as a reticulum, or scattered granules.

3. *Microscopic Study.* The most striking feature of the stools, apart from the parasites, lies in the presence of enormous numbers of large and small, motile and non-motile bacilli or spirillæ. Indeed, such great numbers of bacteria often urge one on to examination of many specimens for protozoa when the first slides have proved negative. Frequently the bacteria are so numerous as to resemble a hanging-drop from a bacterial culture.

In addition to bacteria are generally noted actively budding yeasts, chains or groups of cocci or of torulæ, scattered collections of mucous corpuscles or leukocytes and occasional, usually partly degenerated, red blood cells. In some smears, ammonium triple phosphate crystals and leucin plates and fatty acid needles are often very abundant. There are generally considerable undigested vegetable tissue and partly broken-up muscle bundles when the patient has been on a fairly full diet.

4. *The Protozoa.* As already stated persistent search is often necessary before the organism can be properly seen and identified. This applies particularly to entamebæ; the flagellates are readily recognized by one with the common training in parasitology. There is still considerable debate respecting the identity of entamebæ histolytica and tetragena. We have followed the classifications of Darling and of Craig in considering the cellular variations to represent different stages of the same organism. The histolytica stage appears to represent the organism at its maximum of activity and probably pathogenicity.

In our series of cases the incidence of the protozoa was as follows:

TABLE IV.

Cercomonas intestinalis hominis	36
Trichomonas intestinalis hominis	21
Entamebæ—Histolytica stage	17
Tetragena stage	6
Unclassified	4
Entamebæ total	27
Lamblia intestinalis hominis	5
Megastoma entericum	2
Balantidium coli	2
Grand total of cases	93

COINCIDENT INFECTIONS.

Cercomonas with entamebæ	12
Trichomonas with entamebæ	14
Cercomonas, trichomonas and entamebæ	4
Trichomonas and cercomonas	8
Cercomonas and lamblia	3
Cercomonas, trichomonas and lamblia	2
Trichomonas, cercomonas and megastoma	1
Trichomonas and balantidium	2

5. *Chemical Examination of the Stools.*

(a) *Blood.* Altered blood was demonstrated in 74 instances (79 per cent.) by the benzidin test.

(b) *Pancreatic Efficiency Tests.* Quantitative estimation of trypsin and amylase was made by the methods of Gross-Fuld-Wohl-gemuth in 29 cases. In 22 instances (76 per cent.) trypsin was reduced below the normal (500 units). In 9 instances (31 per cent.) amylase was deficient.

(c) *Bile Pigment.* By the Schmidt bichloride test made upon stools from 46 individuals, bilirubin was present in 32 (69 per cent.) and biliverdin in 14 (30 per cent.).

6. *Gastric Analyses.* It is not infrequently stated that when protozoa are found chronically in the stools of patients of the temperate zone, such are secondary contaminations due to gastric achylia. It has not been shown why if such be the case there should not be a more universal finding of protozoa in the great group of achylia that come under observation. It is not unlikely that the rapid multiplication of protozoa and symbiotic bacteria in the intestinal canal is capable of bringing about toxic gastric or pancreatic achylia. Similar occurrences have been noted in association with typhoid fever and pellagra in our clinic and in cholera and intestinal tuberculosis by others.

In our series there were 40 cases (43 per cent.) with gastric achylia; 33 cases (36 per cent.) and subnormal hydrochloric acidity and 20 cases (21 per cent.) with normal or increased gastric HCl. In one instance of most pronounced acute infection with cercomonads and trichomonads the free HCl was 86.

The gastric motility was normal in 83 cases (89 per cent.). In 10 cases (10 per cent.) there was mild stagnation.

7. *Anemia.* In 19 instances this was sufficiently striking to suggest pernicious anemia. Study of numerous blood counts and films failed, however, to establish the disease. The characteristic anemia is of secondary type, such as is common in chronic intoxications, namely, nephritis, cancer or malnutrition. The average *hemoglobin* was rather more than 70 per cent. The average red cell count was 3,120,000. The average white cell count was 8400. The *differential counts* revealed no great abnormality apart from the tendency of the small lymphocytes to increase at the expense of the polynuclears and, in some instances, a rather high percentage of eosinophiles. There were 69 cases (74 per cent.) where the eosinophile percentage equalled or exceeded 3. There were 11 instances where it ranged between 8 per cent. and 14 per cent. In 1 case the eosinophiles reached 18.5 per cent. (an instance of amebiasis and trichomoniasis). The blood counts are liable to show higher eosinophile counts before purgation than afterward. It was not observed that blood from cases presenting clinical signs of grave intoxication gave the highest eosinophile counts: in fact the most

pronounced eosinophilias were recorded in young individuals who had presented symptoms of protozoic infection for but a few years.

8. *Urine.* In 16 instances albuminuria was noted. It is not possible to state that this finding was directly due to the presence of parasites. Many of the cases were at the age in life when traces of albumin are quite commonly found in the urine.

E. TREATMENT.

1. *General.* It is important that all local infection foci (teeth, tonsils, mouth or throat ulcers, diseased gall-bladders or appendices, etc.) should be removed before attack is made upon the intestinal infection. If such are not taken care of radically, reinfections may occur or subsequent ailments of such parts may lower general resistance sufficiently to again permit of enteric infection by protozoa. Encysted protozoa may lurk for years in the appendix or the gall-bladder. When such is the case the host is to be considered a not altogether harmless carrier.

2. *Measures to Free the Intestine of Protozoa.* A preliminary preparation of the intestinal canal enables one to quickly bring about its sterilization. In my clinic these patients are placed upon a liquid diet for two days before medical care is begun. This permits of the bowel being freed from firm residues. Each morning they receive a glass of citrate of magnesia solution. *The aim of specific medicines is to render inert protozoa infecting the intestinal contents and thus prevent infections of the mucosa and to destroy organisms already lodged within the mucous membrane.* Successful therapy depends upon proper isolation of the infecting parasites: entamebæ are particularly susceptible to ipecac or its alkaloid, emetin, while flagellate or ciliated protozoa are slightly affected by these drugs but are readily destroyed by calomel. Thymol is effective against both parasites.

(a) *In the entamebæ cases* the patient is put to bed on liquid diet, with hot pads moistened in boracic alcohol mixture over the abdomen (to prevent colicky pains or abdominal discomfort). He is then given by mouth a 10-grain tablet of the aluminum salicylate of ipecac ("alcresta") every hour and $\frac{1}{3}$ grain of emetin hydrochloride hypodermically every four hours for two days.¹ If the stools show diminution of the parasites the dose of ipecac and emetin is then reduced by one-third and this continued for another two-day period. No reduction is made if the parasites are still very abundant or are very active. Usually by the end of the first week the patient is taking 1 to 2 grains of emetin hypodermically daily and 10 grains of ipecac ("alcresta") four times daily. The treatment is continued even when no parasites are seen. Accompanying the medicines given by mouth the colon is carefully lavaged with 4 quarts of hot normal salt solution or a solution of quinin, $\frac{1}{3000}$, and thymol,

¹ We have also administered ipecac in the form of salol-coated pills (as suggested in 1903 by Dock), wine of ipecac by the duodenal tube (after Beek's method), and recently 1 to 3 ounces of wine of ipecac directly into the colon *per rectum*. The last procedure seems to offer a therapeutic regime of much value in severe cases.

$\frac{1}{50000}$, in normal salt solution night and morning. On the sixth day the patient is put on fat-free diet for twenty-four hours (to render thymol administration safe). At bedtime of the seventh day 30 grains of thymol in honey are administered at 8 P.M., and again at 10 P.M. At 6 A.M. the following morning the patient gets 2 ounces of Epsom salt in hot water and all that morning frequent drinks of black coffee, fat-free broth or malted milk. During the second week the emetin, ipecac and bowel irrigations are continued, and usually on the tenth day from the beginning of the treatment two doses of 15 grains each of thymol (preceded by twenty-four hours of fat-free diet) are given in the evening. Daily examinations of the warm stools usually indicate no parasites by this time and the diet may be increased according to the patient's desires, provided it is low in protein and not very bulky. If parasites persist at the end of two weeks, then after thorough colon lavage with hot normal saline solution, from 500 to 1000 c.c. of filtered, commercial kerosene are given per rectum, slowly. The external parts are greased with carbolated vaselin and effort is made to have the patient retain the kerosene for at least one hour. We have never seen any harmful effects follow the use of kerosene. It has proved very efficacious in ridding the bowel of persistent infection.

When the entamebæ are no longer demonstrable in the freshly passed stool, then local treatment of the enterocolitis by large doses (30 grains) of bismuth subnitrate or subcarbonate given five times daily should be carried out. Emetin and ipecac should be continued for at least five weeks, the ipecac alone for three months. The bowel irrigations are usually stopped at the end of the third week. The general state of the patient is taken care of according to indication: HCl after meals if the gastric juice is lacking in acid; iron and arsenic if anemia is present.

(b) When *flagellate protozoa* are the infecting organism the treatment is substantially as outlined above for entamebæ except that emetin and ipecac are not used unless there is a concomitant amebiasis. The flagellates are readily destroyed by the administration of evening doses of calomel (5 to 15 grains) followed by 2 ounces of Epsom salt the next day. These doses of calomel are repeated about every five days, according to the indications furnished by the stool examinations. The flagellates are usually less persistent than are the entamebæ with the exception of lamblia.

(c) *After-treatment.* Our study of specimens of gall-bladders and appendices removed at laparotomy indicates that in these parts of the gut cysts of protozoa may lurk for years. Reinfection of the bowel is thus possible. Consequently if these organs have not been removed we insist that our patients have stool examinations at least three times a year and that they go through an abbreviated course of treatment similar to that above outlined. Only in this way do we believe that protozoa "carriers" can be eliminated or reinfection of so-called cured cases prevented.

REFERENCES.

1. Sistrunk: Jour. Am. Med. Assn., November 4, 1911, p. 1507.
2. Freund: Arch. Int. Med., 1908, No. 1, i, 68.
3. Sanford: Wisconsin State Med. Jour., April, 1914.
4. Sanford and New: Surg., Gynec. and Obst., January, 1916, p. 27.
5. Giffin: Jour. Am. Med. Assn., August 30, 1913, p. 675.
6. Rhamy and Metts: Jour. Am. Med. Assn., April 15, 1916, p. 1190.
7. Chase: Jour. Am. Med. Assn., May, 1917.
8. Smithies: Med. Clin. of Chicago, May, 1917, No. 6, ii, 1109.
9. Schultz: Jour. Am. Med. Assn., September 30, 1911, 1102.
10. Jones: Jour. Am. Med. Assn., March 20, 1915, p. 982.
11. Darling: Tr. Fifteenth International Congress on Hygiene and Dermography, September 23, 1912, p. 28.
12. Craig: Arch. Int. Med., June, 1914, p. 1917.
13. Deeks: Jour. Am. Med. Assn., January 4, 1913, p. 38.
14. Beck: Jour. Am. Med. Assn., December 14, 1912, p. 2110.
15. Brem and Zeiler: AM. JOUR. MED. SC., November, 1910.

EFFECT OF STIMULI FROM THE LOWER BOWEL ON THE RATE OF EMPTYING THE STOMACH.¹

BY FRANKLIN W. WHITE, M.D.,

INSTRUCTOR IN MEDICINE, HARVARD UNIVERSITY; VISITING PHYSICIAN, BOSTON CITY
HOSPITAL, BOSTON, MASSACHUSETTS.

It has been shown by Cannon² and others that irritation of the colon may delay the emptying of the stomach. This is striking and well known when powerful stimuli occur, as in intestinal injury, in cutting, drying or handling the bowel. Here there is a definite protective mechanism holding back food above until some measure of healing occurs below.

Some men have also emphasized the effect of distention or irritation of the lower bowel by enemata, stasis in the ileum, inflammation of the appendix, adhesions in the ileocecal region, etc., in causing the stomach to empty slowly (Hirsch,³ Alvarez,⁴ Baumstark,⁵ Jordan,⁶ Eisen,⁷ Smithies,⁸ Barclay,⁹ Cole,¹⁰ Ochsner,¹¹ Borbjarg¹²). We have studied a group of such cases to find out how frequently this occurs and what sort of irritation gives this result. We have a series of clinical observations and also of animal experiments.

¹ Read at the thirty-second Annual Meeting of the Association of American Physicians, Atlantic City, May 2, 1917.

² The Mechanical Factors of Digestion, London, 1911.

³ Centralbl. f. klin. Med., 1893, xiv, 377.

⁴ Jour. Am. Med. Assn., 1915, lxxv, 388.

⁵ Ztschr. f. physiol. Chem., 1910, lxxv, 484.

⁶ Archiv. Roentg. Ray, 1913, xviii, 231.

⁷ Jour. Am. Med. Assn., 1914, lxxiii, 1228.

⁸ AM. JOUR. MED. SC., 1915, cxlv, 187.

⁹ The Alimentary Tract, New York, 1915.

¹⁰ AM. JOUR. MED. SC., 1914, cxlviii, 109.

¹² Arch. f. Verdauungskr., 1911, xvii, 706.

¹¹ Ibid., 1906, cxxvii, 1.

Our results all point definitely the same way. (1) Regarding *frequency*, delay in emptying the stomach is the exception, not the rule, in lesions of the lower bowel; (2) regarding the *kind of irritation*, a strong stimulus is needed from the lower bowel to slow the stomach.

TECHNIC OF OBSERVATIONS. We judged the time of emptying the stomach by watching the progress of a barium meal with the roentgen rays and fluorescent screen in men and cats. A carbohydrate meal was chosen because it favors prompt emptying of the stomach; we used potato gruel, mixed with barium sulphate, in the proportion of 100 gm. of barium to 500 c.c. of gruel. We gave a 500 c.c. meal to the men and 25 c.c. to the cats and studied the residues in the stomach after five or six hours in men and after two or three hours in cats.

We tried to avoid other factors causing delay in emptying the stomach, such as emotion, trauma, etc. For example, we might expect that fastening a cat to a holder, giving a meal by the stomach tube and then a rectal injection would produce such unpleasant emotions that observation on the time of emptying the stomach would have little value. We used elderly female cats and found that with a little practice these things could be deftly done within a few minutes, and the psychology of these cats is such that, if kindly treated, they were purring and contented within a minute or two after release from the holder. For later roentgen-ray examinations no holder was needed.

Operative trauma, the use of a fistula or injections through the peritoneum into the bowel were avoided by simply passing a catheter per rectum through the colon up to the cecum and making injections through this; with the colon empty and a catheter of proper size and flexibility (No. 16 French) this is easily done under the fluorescent screen. Irritants to be injected were usually mixed with a little barium sulphate and the injection also made under the fluorescent screen to control how much was given and exactly where the injection was placed.

THE EFFECT OF MECHANICAL FILLING OR DISTENTION OF THE COLON. The men were given by mouth 500 c.c. of barium potato gruel. The cats were fed by the stomach tube with 25 c.c. of the gruel. The cats were released at once and were not examined for two or three hours. In men bland rectal injections of 1000 to 1500 c.c. of potato gruel were given and retained as long as possible—usually from one to one and a half hours. In cats a similar rectal injection of 30 c.c. to 40 c.c. was used.

This had little or no effect upon the emptying of the stomach. Food passed steadily through the pylorus while the enema was retained and the stomach was entirely empty within the normal period in each of the 10 cases in which this was tried. The only effect was a slight delay in the action of the stomach for the first

few minutes. This does not agree with the statement of Alvarez that introduction of food at the lower end of the digestive tract markedly retards the progress of material coming down from above.

The fact that patients occasionally vomit after rectal feeding is poor evidence of reflex action from the colon to the stomach, because rectal feeding is usually given on account of *previous* vomiting in gastric ulcer, stenosis, etc., and the fact remains that most patients do *not* vomit after rectal feeding.

THE EFFECT OF STASIS IN THE ILEUM. Out of a group of more than 200 patients in whom roentgen observations were made six and twelve hours after a barium-potato gruel meal, there were 42 without important lesion of the stomach whose small intestines emptied slowly and who had residue in the ileum at the end of twelve or more hours. In 16 the twelve-hour ileal residue was large, in 3 cases, persisting until nineteen, forty-eight and fifty-four hours respectively, in 18 was moderate and in 8 small; the lesion was chronic appendicitis in 20; adhesions of the ileum or colon in 20; atony and ptosis in 10; diseases of the gall-bladder in 2.

Only 4 of these cases showed any delay in emptying the stomach as measured by a six-hour residue.

In 2 the stomach residue at the end of six hours was very small and both were delicate women over seventy years, in whom a slight delay was not remarkable. The other 2 with good-sized residue showed slight deformities near the pylorus, which we interpreted as possible adhesions or spasm.

In short, in nearly all the cases which showed definite or marked delay in emptying the small intestine the stomach emptied promptly. This does not seem to support Barclay's theory of an ileopyloric reflex from the last coils of the ileum to the pylorus to shut off the food supply by closing the pylorus until the ileum is more empty.

The pyloric spasm seen by radiologists in chronic appendicitis is variable and uncertain and has little constant effect on function, the more chronic and quiescent the appendix the less likely it is to cause delay.

Smithies found persistent gastric retention in only a little over 3 per cent. of pyloric spasms associated with appendicitis and cholecystitis; intermittent retention was frequent and usually disappeared after removal of the appendix or gall-bladder.

EFFECT OF CHEMICAL IRRITATION OF THE BOWEL. This was tested in cats in the following way: In order to produce irritation in the cecum without any other trauma to the bowel a well-oiled rectal catheter was passed up the colon to the cecum and the irritant injected with a syringe. The short, simple colon of the cat makes it easy to pass a catheter, and its exact location was shown with the fluorescent screen. Barium sulphate was mixed with the injected material so that the amount and place of the injection could be seen.

Twenty-five successive experiments with two different cats showed

that injection of turpentine oil, either a few drops or ten drops or 2 c.c., caused no delay in emptying the stomach. The same result was obtained with a few drops of croton oil. Injection of 4 or 5 drops of mixtures of mustard oil and olive oil gave varied results: in 4 instances the cat vomited the whole contents of the stomach promptly after the injections, in 4 cases the injection slowed the emptying of the stomach, evidently in proportion to the strength of the mustard oil and the irritation produced in the colon: that is, the emptying time of the stomach was delayed from the normal two or three hours to five or six hours. In striking contrast to this, active irritation of the cecum with mustard oil caused *just as often* rapid downward emptying of the stomach and the whole digestive tract both above and below the irritated point.

We may grade the results roughly according to the degree of irritation of the cecum.

1. Intense irritation caused prompt reverse peristalsis in the stomach, with vomiting of its whole contents.

2. Marked irritation caused either (*a*) delay in emptying the stomach up to about twice the normal time, evidently due to spasm of the pylorus, or (*b*) hyperperistalsis and rapid emptying of the stomach and the whole digestive tract.

3. Moderate or slight irritation had no effect on the emptying of the stomach.

We did not get a perfect gradation of results, evidently because of the part played by spasm, which was very variable.

CLINICAL DATA IN DISEASE OF THE LOWER BOWEL. Data in the following group of intestinal cases show that delay in emptying the stomach after a barium meal is the exception not the rule. We need to be careful in studying such a group to allow for some delay due to ptosis and atony of the stomach, which often occurs in thin, weak or old people:

In 7 cases of chronic colitis there was no delay in emptying the stomach. In 3 cases of tubercular ulceration of the colon there was no delay and the diseased part of the bowel was so irritable that the barium meal passed through it very rapidly and it appeared empty. This is typical of this disease.

In 5 cancers of the colon, causing more or less obstruction, 2 of the cecum and ascending colon, 2 of the transverse colon and 1 of the sigmoid, there was no delay. In 1 case of chronic intussusception of the ileum one foot above the ileocecal valve there was no delay. Borbjarg in studying tumors of the ileocecal region and colon (using the residue six hours after a Riegel meal to test gastric motility, possibly an overduplicate test) suggests that tumors below the cecum do not delay stomach emptying and that tumors in the ileocecal region frequently do.

We have seen that in 42 cases with ileal stasis occurring in chronic appendicitis and adhesions of the ileum and colon only 4 showed any

delay in emptying the stomach. In an additional group of 53 cases, 27 with clear evidence of chronic changes about the appendix, 26 with adhesions of the ileum, cecum or colon, there were only 3 which showed any delay in emptying the stomach; 1 was a case of chronic appendicitis and 2 adhesions. There was 1 medium and 2 small five- to six-hour residues.

We had little chance to study acute appendicitis because early operation is usually needed. Two out of 8 cases of acute and sub-acute appendicitis showed slight delay in emptying the stomach, namely, a small six-hour residue, with the stomach empty at the end of seven or eight hours. This was not conclusive, as we obtained the same result in several other fever cases, with pain in which the bowel was not involved. Our experience with chemical irritants of the cecum suggest that different degrees of inflammation of the appendix may affect the stomach in a corresponding way by causing vomiting or delay in emptying or rapid emptying, though we have not been able to prove it.

Peritoneal involvement is important. Compare the definite effect on the stomach which Cannon¹³ got by performing a laparotomy and injecting croton oil into the cecum by needle through the peritoneum; with the lack of effect we obtained by avoiding the peritoneum and injecting the croton oil by catheter. The element of pain is important—even such a simple lesion as fissure of the anus, if very painful, may cause delay and a good-sized six-hour residue in the stomach.

In a total of 120 cases of lesions of the lower bowel there were only 9, or 7.5 per cent., which showed any delay in emptying the stomach. Several of these cases were old and weak and some delay might be expected independent of reflexes from the lower bowel.

Clinical and experimental observation in lesions and irritation of the *upper* bowel (duodenum and jejunum) have shown that they often delay emptying of the stomach; they are outside the scope of this paper.

In conclusion, there is evidently a definite correlation of upper and lower parts of the digestive canal by a protective mechanism which works under a powerful stimulus, such as intestinal injury or surgery or intense irritation, but which does not work under a moderate stimulus or simple mechanical condition. The action of this mechanism is complicated by the contrary results of spasm and hyperperistalsis.

Evidence indicates that the delay in emptying the stomach is the result of impulses through the vagus causing pylorospasm, not inhibition of the motor fibers of the stomach through the splanchnic nerves.

The delay in emptying the stomach caused by spasm of the pylorus is very variable, present one day and absent the next, under similar conditions; in general, *marked delay* in emptying the stomach

¹³ The Mechanical Factors of Digestion, London, 1911.

is far more often the result of actual lesions about the pylorus than of reflexes from the bowel.

It is not fair to compare the intestine to a railroad under a block system, where delay low down the line regularly holds up food for several blocks above or to say that "an irritating lesion slows the progress of food coming toward it from above." It may or may not do so, depending on the character and degree of the irritating lesion. It is evident that "stomach symptoms" in intestinal cases are not the result of slow emptying of the stomach, as a rule, but are largely toxic or the result of referred pain or distress.

SUMMARY. The roentgen-ray method was used to study the effect of stimuli from the lower bowel on the rate of emptying of the stomach; the effect of mechanical filling and distention of the colon by enemata in men and cats; the effect of chemical irritation of the cecum in cats; the effect of diseases of the lower bowel in 120 cases of chronic colitis, tubercular ulceration and cancer of the colon, chronic and acute appendicitis and adhesions of the lower ileum and colon.

Our results all point the same way: (1) delay in emptying the stomach is the exception, not the rule, in lesions of the lower bowel; (2) a strong stimulus is needed from the lower bowel to slow the stomach, for it was found that the stomach emptied a barium meal within the normal time in some cases of ileal stasis of two or more days' duration, and in most cases with good-sized twelve-hour residue in the ileum, also when the colon was distended with a large enema, also in most cases of chronic appendicitis and chronic inflammations and tumors of the colon.

Experiments on animals showed that when the colon was irritated by injections into the cecum variable results were obtained; intense irritation caused vomiting; less marked irritation caused either delay in emptying the stomach up to about twice the normal time or rapid emptying of the stomach and whole digestive tract; moderate or slight irritation had no effect. The results were not perfectly graded, evidently because of variable spasm.

There is evidently a definite correlation of different parts of the the digestive canal by a protective mechanism which works under a powerful stimulus, such as intestinal surgery or injury or strong irritation, but which does not work under a moderate stimulus or simple mechanical condition. The action of this mechanism is complicated by the contrary results of spasm and hyperperistalsis.

Marked delay in emptying the stomach is far more often the result of actual lesions about the pylorus than of reflexes from the bowel. "Stomach symptoms" in intestinal cases are not, as a rule, the result of slow emptying of the stomach.

I wish to acknowledge my indebtedness to professor Walter B. Cannon, of Boston, for valuable help and suggestions, and to Dr. L. B. Morrison, of Boston, for roentgen-ray data in some of the intestinal cases.

PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX.

A REPORT OF 12 NEW CASES OCCURRING IN 10,651 SPECIMENS, WITH
A SUMMARY INCLUDING 5 PREVIOUSLY REPORTED CASES
AMONG 2500 SPECIMENS.

BY STANLEY P. REIMANN, M.D.,
PHILADELPHIA, PA.

(From the Department of Pathology of the Lankenau Hospital, Philadelphia, Pa.)

CASES of primary carcinoma of the vermiform appendix to the number of almost 300 have been reported and a number of characteristics of this neoplasm has been revealed. It occurs more commonly in the female, occurs in younger rather than older persons; it has never been diagnosed clinically and seldom grossly; it is clinically usually benign, but malignant results have been reported; it is found in from 0.33 per cent. to 1 per cent. of appendices examined; it is almost always associated with some form of inflammation. It occurs in two main histological varieties, a form with small cells and usually much fibrosis, and a cylindrical-cell type resembling carcinomata of other parts of the intestinal tract.

In 1900, and again in 1908, Kelly¹ reported cases of primary carcinoma of the appendix from this laboratory, occurring among 2500 appendices examined. Since that time 12 more have been discovered in the routine examination of 10,651 more specimens as they came from the clinic of Dr. John B. Deaver. Short histories and abbreviations of the pathological reports and a summary of findings in the light of what has been revealed by the reported cases will be given. Mention of cases reported by Kelly will be included for the sake of completeness. In Case No. 4 of his first series doubt is expressed of the origin of the tumor, so it will not be included in this series. In 1 case the clinical history was lost, so that in the summary of clinical facts, 16 cases will be considered. To simplify classification the tumors will be grouped under two main types which, when reports are analyzed, can be recognized as the important ones, viz., the small-cell type and the columnar-cell type.

CASE I (1898).—The clinical history was lost. Grossly the appendix showed gangrenous inflammation, with the distal two-thirds less involved but thicker than the proximal portion.

Histologically there was a high-grade ulcerative process present. A tumor about 6 mm. in diameter in the mucosa and submucosa was

¹ Kelly, A. O. J.: Tumors of the Vermiform Appendix, Proc. Path. Soc. of Philadelphia, 1900, new series, vol. iii. Primary Carcinoma and Endothelioma of the Vermiform Appendix, AM. JOUR. MED. SC., 1908, vol. cxxxv, 851.

found toward the distal end, and it consisted of nests of epithelial cells in a connective-tissue framework.

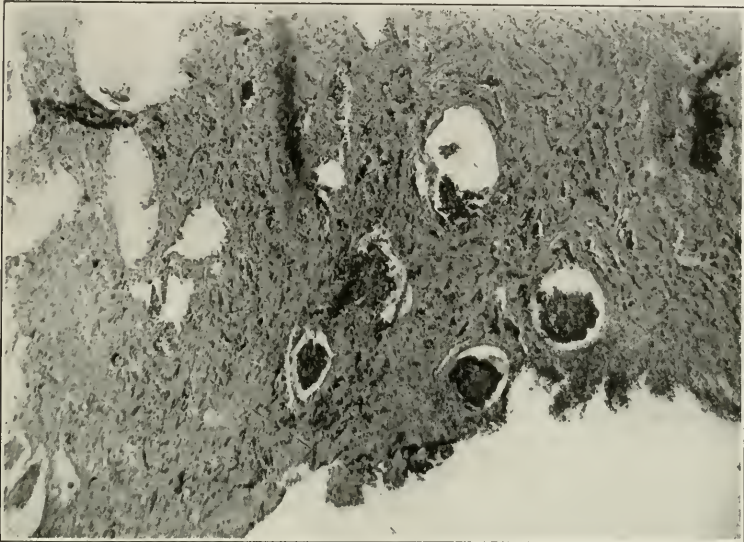


FIG. 1.—Photomicrograph of the small-cell type, showing nests and groups of small more or less rounded epithelial cells in the submucosa. The mucosa is completely ulcerated.

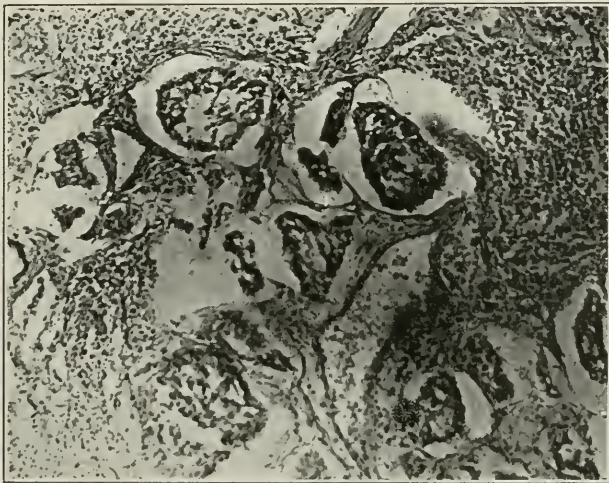


FIG. 2.—Photomicrograph of the columnar-cell type, showing groups of larger, more or less columnar cells in the submucosa, with a hint at "adeno" arrangement.

Diagnosis: Primary small-cell carcinoma of the appendix; acute ulcerative appendicitis.

CASE II (1899).—J. M., male, aged nineteen years.

He had pain eight days previous to admission. At operation a small encapsulated abscess at the appendix was found. Grossly a fibrinous exudate covered the appendix which, when pulled off, left the organ much distorted.

Histologically an ulcerative process was found and a small tumor in the submucosa toward the base, which was composed of nests of small epithelial cells in connective-tissue framework.

Diagnosis. Primary small-cell carcinoma of the appendix; acute ulcerative appendicitis.

CASE III (1906).—S. B., married woman, aged twenty-three years.

Operated by Dr. Deaver for acute appendicitis. The appendix was kinked on itself and curled about the cecum. A new growth invaded all the walls from the tip almost to the proximal end.

Histologically it consisted of nests of epithelial cells exhibiting mucoid degeneration. Evidences of chronic interstitial inflammation with acute exacerbation, were found.

Diagnosis: Primary small-cell carcinoma of the appendix; acute exacerbation of chronic interstitial appendicitis.

CASE IV (1907).—L. B., single woman, aged twenty-seven years.

Symptoms were referable to the upper right hypochondrium, and Dr. Deaver examined the gall-bladder region, where no abnormalities were found. The appendix was then removed through a separate incision. A bulbous enlargement was found at the distal end.

Histologically, nests of epithelial cells supported by well-developed connective-tissue stroma were found, which invaded the submucosa and muscularis. Chronic interstitial inflammatory changes with acute exacerbations were also found.

Diagnosis: Primary small-cell carcinoma of the appendix; acute exacerbation of chronic interstitial appendicitis.

CASE V (1908).—M. K., single woman, aged twenty-eight years.

Dr. Deaver operated for appendix abscess and found considerable pus and a perforated appendix. No evidence of new growth was found grossly, and even after it was discovered microscopically it could not be located by the unaided eye. It was annular and occupied the dilated peripheral extremity. Nests of epithelial cells in a well-developed connective-tissue stroma invaded submucosa and muscularis. Acute inflammatory changes of usual type were present.

Diagnosis: Primary small-cell carcinoma of the appendix; acute diffuse suppurative appendicitis.

The new cases are reported in more detail.

CASE VI (1908).—R. S., single woman, aged nineteen years.

Family and past histories were entirely negative. She has had recurrent attacks of pain in her right iliac fossa, lasting from a half

to twelve hours, since an acute attack which lasted three weeks, three months before admission. No vomiting.

Physical examination showed no abdominal tenderness at the time, but she pointed to McBurney's point as the seat of the pain. Temperature normal, white blood cells 12,800 with 81 per cent. polynuclears. Dr. Deaver operated, removing a swollen appendix. Uneventful recovery.

Appendix with a small portion of the mesentery 6 x 0.8 cm., bulbous enlargement 1.2 cm. in diameter at the tip. The serosa was covered with fibrinous exudate. Walls were edematous and the mucosa swollen. Section through the bulbous tip showed obviously a tumor of firm consistency invading from the mucosa outward to the serosa.

Histologically the serosa was covered by a fibrinopurulent exudate, showing beginning organization. All the coats were diffusely infiltrated by pus cells, vessels were intensely congested and there was considerable edema. Mucosa ulcerated, a few glands remaining showed mucoid degeneration. A new growth occupied the position of the submucosa and infiltrated the muscularis to a slight extent in only one portion of the circumference. It consisted of nests of more or less degenerated cells in well-defined groups of twenty to fifty embedded in a loose edematous connective-tissue framework. There was a hint at "adeno" arrangement. The individual cells were columnar, epithelial in character and showed marked cloudy swelling, with here and there pyknosis of nuclei and necrosis. The cytoplasm of the better preserved cells was abundant and stained well, and the nuclei were round and rich in chromatin.

Diagnosis: Primary columnar-cell carcinoma of the appendix; acute diffuse suppurative appendicitis.

CASE VII (1909).—F. A., male, aged twenty-six years, married. Iron molder.

His father had had an arm amputated for cancer of the hand, and had died subsequently of "stomach trouble."

The patient had always been well with the exception of two attacks, eighteen and twelve months before, similar to the one which brought him to the hospital. The morning after a drinking bout he was seized with sudden, severe pain in the "pit of his stomach, which soon localized to his right iliac fossa, where it remained constant and severe and was not controlled by ice. Vomited several times. Temperature on admission was 99.4°; white blood cells numbered 11,300, with 66 per cent. polynuclears.

Physical examination showed a flat abdomen, rigid and tender in the right iliac fossa. No masses were discovered. Dr. Deaver removed a greatly inflamed appendix covered with exudate. Uneventful recovery.

Appendix 9 x 1 cm., with small portion of mesentery. The serosa was covered with fibrinous exudate, deeply congested. Walls thick-

ened and edematous, mucosa desquamated and partly gangrenous. Lumen patulous. Contents sanguinopurulent. About the distal third was a small area of thickening and induration almost annular.

Histologically the serosa was covered with a hemorrhagic fibrinopurulent exudate. A few pus cells and eosinophiles were scattered in the muscularis and submucosa. The mucosa was completely ulcerated. In the submucosa and invading the muscularis down to the serosa was a new growth consisting of small nests of cells embedded in dense cellular connective tissue in the submucosa and invading the muscularis in tissue spaces and between muscle bundles. The cells were small epithelial in type, well stained, with large round nuclei rich in chromatin.

Diagnosis: Primary small-cell carcinoma of the appendix; acute ulcerative appendicitis.

CASE VIII (1909).—M. R., married woman, aged thirty-two years.

Her family history was negative. She had had pneumonia at fourteen years and rheumatic fever at twenty-four. "Epigastric discomfort," "puffed feeling," occasional belching and heartburn were experienced for some time. Ten days before admission she was taken with sudden cramp-like pains in her right iliac fossa, accompanied by nausea and later by vomiting. They remained for seven days, when they subsided, but soon returned in the right pelvic region as well as around McBurney's point. Temperature, 99.6°; white blood cells, 10,900; polynuclears, 70 per cent.

Physical examination showed a rigid abdomen, with marked tenderness over McBurney's point. No masses were felt. Tenderness was also present in the right pelvic region.

Dr. Deaver found the appendix pointing toward the pelvis, constricted in the center, ballooned and tense at the tip, with marked serous exudation. Microscopically the serosa and the muscularis showed some edema. Occupying the position of the submucosa, mucosa, and obliterating the lumen was a tumor consisting of nests of epithelial cells, which invaded the muscularis to the serosa. The nests were embedded in loose, highly cellular connective tissue except in the muscularis, where they lay in tissue spaces and between muscle bundles. The cells were arranged more or less in gland-like form, with several rows around an attempt at a lumen; the individual cells were more or less cylindrical, with a fair amount of cytoplasm, lightly stained and highly granular. Nuclei were rounded and vesicular.

Diagnosis: Primary columnar-cell carcinoma of the appendix; acute serous appendicitis.

CASE IX (1911).—E. C., married woman, aged twenty-five years.

Family and past histories entirely negative. Two years before admission she noticed pain in the epigastrium, which at times became severe enough to "take her breath." It came about every two weeks, about two hours after meals, and lasted for about three

hours. Taking of food had no influence so far as she knew. She never was nauseated, never vomited nor belched. The pain never occurred in the right iliac fossa. Never jaundiced.

Physical examination showed no tenderness in the abdomen at the time. Pelvic examination revealed a small hard cervix, retro-displaced uterus and tenderness on pressure along the neck of the uterus. Dr. Deaver removed an appendix, adherent and bound to the subcecal fossa. At the same time her cervix was dilated, the uterus brought forward and a small portion of the right ovary excised with a small cyst. Stones were removed from the gall-bladder and a cholecystostomy performed. Uneventful recovery.

Grossly the appendix showed a thickening which was obviously a new growth, hard and firm, occupying about half the circumference opposite the mesenteric attachment and extending almost the entire length of the organ.

Microscopically the serosa was normal. The musculature showed hyalinization and considerable lymphocytic infiltration. Replacing the mucosa and submucosa was a tumor consisting of strands and chains of cells of epithelial type which penetrated the muscularis to the serosa. The individual cells were small, rounded, with scanty light-staining protoplasm and round vesicular nuclei.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic interstitial appendicitis.

CASE X (1911).—E. L., seamstress, single, aged twenty years.

Family and past histories negative. Six months before admission she had acute, lower right abdominal pain, followed by vomiting and associated with tenderness, localized to the same region. She remained in bed for two weeks and afterward experienced pain of a drawing character in the appendix region until two weeks before admission, when acute pain returned, with vomiting. She again remained in bed, this time for four days, the tenderness persisting until admission.

Physical examination showed slight tenderness and voluntary rigidity over the right iliac fossa. Temperature, 99.4°; white blood cells, 6500; polynuclears, 58 per cent.

A thickened appendix was removed by Dr. Deaver.

Grossly the appendix gave no evidence of a new growth. The walls were slightly thickened, the coats obscured and the mucosa swollen.

Microscopically the serosa was thickened and the muscularis showed large areas of hyaline degeneration and considerable lymphocytic infiltration. Infiltrating the entire thickness over the whole circumference and up to the serosa was a tumor of large and small strands and chains of epithelial cells which penetrated in all directions. The cells were small, more or less circular, with small amounts of cytoplasm and relatively large dense nuclei. There were areas in the submucosa in several sections which were solid tumor masses.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic interstitial appendicitis.

CASE XI (1912).—H. H., tailor, married, aged thirty-four years.

Family and past histories were entirely negative. He entered the hospital to have a hernia of one and one-half years' duration repaired. Had no symptoms of any kind except the presence of the hernia.

Physical examination was negative except for a complete indirect right inguinal hernia.

Dr. Deaver removed a long, thick, stiff appendix and performed a herniorrhaphy. Uneventful recovery.

Appendix with small portion of mesentery, 9 x 0.8 cm. The serosa was slightly congested. The lumen was eccentrically placed, closer to the mesenteric attachment than to the opposite serosa. The thicker portion of the wall was 0.5 cm. thick, tough, firm and showed no differentiation of mucosa, submucosa and muscularis for a distance of 3 cm. in the middle portion. Distally and proximally the coats were distinguishable. Mucosa slightly swollen. Contents mucous.

Histologically the serosa was not thickened. Some evidence of chronic inflammation in a sparse scattering of lymphocytes in the submucosa and muscularis was seen. The mucosa showed a slight catarrh. A new growth invaded the submucosa and muscularis down to the serosa, consisting of small groups of cells thickly scattered in moderately dense connective tissue in the submucosa and invading the lymph channels, and between the muscle bundles in the muscularis. Cells are epithelial in type, rather small, polyhedral, fairly well stained and with densely stained nuclei.

Diagnosis: Primary small-cell carcinoma of the appendix; mild chronic interstitial appendicitis.

CASE XII (1913).—A. G., married woman, aged forty-five years.

Family and past histories were negative. Was operated in 1911 and a large stone removed from the gall-bladder, which was drained and sutured to the parietal peritoneum. Four months after the operation, during which interval she was well, she commenced to have dull, dragging pain with soreness in the upper right quadrant about the site of the scar. A year after the operation nausea and vomiting after eating were added to her symptoms. She had much headache, languor, sleeplessness, and was obstinately constipated.

Physical examination showed an indurated and contracted scar, very tender. No pelvic or appendicular tenderness.

Dr. Deaver excised the scar and released many adhesions. The appendix, adherent to the cecum posteriorly and containing fecal concretions, was removed. Recovery.

The history before her first operation was as follows: Chief complaint: spells of pain in the upper right abdomen. For eight years she had been having several attacks a year of cramps in her

upper right abdominal region, which lasted about fifteen minutes and were not associated with any indigestion; but as the attacks grew more frequent and more severe, belching, heart-burn and flatulence occurred. She was never jaundiced and did not vomit.

Appendix with mesentery excised, 3 x 0.6 cm. Tip bulbous, with the lumen obliterated. Serosa slightly congested, wall thickened, mucosa swollen. Lumen narrowed to bulbous tip, where it was obliterated. Contents mucous. New growth not suspected grossly.

Histologically: Serosa was slightly thickened. Muscularis was atrophied and showed broad bands of hyaline degeneration. Mucosa absent. Obliteration of the lumen had taken place in the bulbous portion by hyalinized connective tissue, in which a small new growth was localized.

The tumor consisted of small nests of more or less degenerated, small epithelial cells, which stained poorly in both cytoplasm and nuclei and invaded the submucosa up to the muscularis but did not penetrate the latter coat.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic obliterating appendicitis.

CASE XIII (1915).—Y. S., married woman, aged fifty-four years.

Family and past histories indefinite. She had slight indigestion for about six months before admission, appearing shortly after eating. For three months previous to admission she had noticed she was growing yellow, and at the same time began having attacks of severe cramp-like pains in her upper right abdomen which radiated to her back and right shoulder and came at intervals of about two weeks and often required "medicine" for relief. Lost much weight.

Physical examination showed moderate jaundice and slight tenderness in the right hypochondrium.

Dr. Deaver found a large tense gall-bladder, which when opened yielded a large quantity of very dark bile and numerous small stones. The common duct was enlarged; it was opened, a probe passed into the duodenum and a T-tube was sewed in for drainage. The appendix was removed through the same incision. The pancreas was described as hard and nodular to the touch.

The T-tube drained well for about a week and the jaundice slowly disappeared, but the tube became clogged and was removed. Reddish-yellow, gritty material filled the tube. The wound drained bile and the jaundice had almost entirely cleared up when the wound closed and jaundice reappeared. This was repeated several times. Pains, chills and fever also accompanied the return of jaundice. Six months after the first operation, Dr. Deaver again opened the abdomen and explored the common and hepatic ducts. Sandy, cement-like material was obtained. Drainage was reestablished but failed in a few days and the patient grew very deeply jaundiced and died in delirium. At a partial autopsy the hepatic and common ducts were found clogged with thick gritty material. Sections of the

pancreas and liver revealed advanced chronic interstitial pancreatitis and periportal cirrhosis of the liver, with acute and chronic cholangitis.

Appendix 8 x 0.3 cm. Small nodule at the tip. The lumen was entirely obliterated.

Histologically: Muscularis was atrophied and showed hyaline degeneration. Mucosa and submucosa were replaced by a tumor consisting of small groups of poorly defined and poorly stained epithelial cells embedded in connective tissue and invading up to but not into the muscularis.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic obliterative appendicitis.

CASE XIV (1915).—F. S., unmarried woman, aged twenty-two years, clerk.

Family history and past history were both negative, except for an abscess of the rectum, which opened through the rectum six months before. She had had occasional pain in the right lower abdomen for about a year, but it was never severe enough to incapacitate her. Two weeks before admission she experienced severe pain, with vomiting, which lasted two days, and subsided only to reappear with greater severity. She vomited during both attacks and had a constant desire to urinate.

Physical examination showed moderate tenderness over McBurney's point.

Dr. Deaver removed an appendix 5 x 0.6 cm., in which the serosa was slightly congested, the walls somewhat thickened and the mucosa swollen. Mucofecal contents: No suspicion of tumor grossly.

Histologically: The serosa was normal. Quite large fat deposits were present between the muscularis and submucosa. Mucosa showed minor changes. Toward the circumference opposite the attachment of the mesentery was a new growth encapsulated almost in its entirety by a thin connective-tissue layer apparently of the submucosa, which was richly sprinkled with lymphocytes. The tumor consisted of large groups of epithelial cells surrounded by a very fine network of connective tissue of younger type in alveolar fashion. The individual cells in the groups were entirely indistinct, the cytoplasm stained lightly, but the nuclei, large, round and vesicular, were quite prominent. Slight invasion of the submucosa was demonstrable in one small area, but the muscularis was free.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic interstitial appendicitis.

CASE XV (1916).—T. K., married woman, aged thirty-five years.

Family and previous histories negative. She had constant pain and soreness in the right side of her abdomen for three years, worse in the right iliac fossa, but also present in her gall-bladder region. It was dull, constant, non-radiating, uninfluenced by food or menstruation, but worse some days than others.

Physical examination showed slight rigidity and tenderness over the gall-bladder region, more marked tenderness to the right and just below the umbilicus. Dr. Deaver removed the appendix for chronic inflammation.

The appendix was 6.5 x 0.7 cm. The serosa was slightly congested the walls somewhat thickened and the lumen obliterated. No macroscopic evidence of tumor.

Histologically: The serosa was normal. Muscularis well preserved. The mucosa was absent. The positions of the submucosa, mucosa and lumen were occupied by masses of epithelial cells embedded in dense cellular connective tissue. The cell masses were very numerous and close together. They stopped short at the muscularis and did not invade any point. Individual cells were small, rounded, with fairly well-stained, scant cytoplasm and large, round, dense nuclei.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic obliterative appendicitis.

CASE XVI (1917).—J. B., married woman, aged thirty-one years.

Family and past histories were negative. Five children living and well. No miscarriage previous to the following: Two weeks before first admission she had a miscarriage, and bleeding continuing, she entered the hospital and a curettage was performed. Bleeding returned in a few days and continued for a month, when she again entered the hospital. During this time she had considerable "soreness" in the lower abdomen. Physical examination revealed slight tenderness over the lower abdomen. No masses. Cervix softened but not dilated; some tenderness to the right side of the uterus. There was a bloody discharge.

Dr. Deaver performed a hysterotomy and removed a small mass of tissue from the cavity of the uterus, which proved on microscopic examination to be decidual tissue. A small fecal concretion was felt in the appendix. Appendix, 7 x 0.6 cm., with the distal 1.5 cm. thickened to 1 cm. The serosa was normal, walls and mucosa slightly thickened. No gross suspicion of new growth.

Histologically: Serosa was slightly thickened; muscular coats were broad and well developed, richly sprinkled with lymphocytes and eosinophiles. Small areas of fat infiltration occurred here and there. There were no typical glands in the mucosa; replacing them were groups and nests of epithelial cells which invaded the submucosa and muscularis up to the serosa. The groups were composed of few rather than many epithelial cells in a fairly dense connective tissue in the submucosa, free in tissue spaces in the muscularis, and the cells were small, generally rounded, with scanty cytoplasm and heavily stained nuclei.

Diagnosis: Primary small-cell carcinoma of the appendix; chronic interstitial appendicitis.

CASE XVI (1915).—Of very special interest is the following case, which occurred in a girl, aged eight years, admitted to the Drexel Home with the diagnosis of acute appendicitis.

Four days before admission she was seized with general abdominal pain, which soon localized and remained in her right iliac fossa. Dr. Deaver removed a perforated appendix which was 7 x 1 cm. long. The serosa was congested and covered with fibrinous exudate; the walls were thickened and the mucosa swollen. Contents were mucopus. Proximally a small localized nodule was found histologically composed of nests of larger epithelial cells arranged "adeno" fashion. They infiltrated to the serosa but were localized to a small area. Pus cells, edema and active congestion were present in the walls.

Diagnosis: Primary cylindrical-cell carcinoma of the appendix. Acute diffuse suppurative appendicitis.

SUMMARY. *Frequency.* In 13,151 appendices examined grossly and histologically, primary carcinoma was found in 17 or about 0.13 per cent. The frequency in reported cases where both gross and histological examinations were made, varies from 0.3 to 1 per cent.

Sex. Reported cases show that about 65 per cent. occur in females. Of the 16 cases with histories in this series, 12 occurred in females, or 75 per cent.

Age. MacCarty and McGrath² report a case in a girl, aged five years, and Rogg³ one in a man, aged eighty-one years. Most of the cases occurred in the second and third decades. The oldest in our group was aged fifty-four years and the youngest eight years. Most of the cases occurred between the ages of twenty and thirty years.

Prognosis. The immediate operative prognosis depends of course on the accompanying lesion, if any, *e. g.*, suppuration, perforation or the trouble for which laparotomy was performed when the appendix is removed incidentally. The great majority of cases reported shows that the condition is essentially benign; metastases and extension have, however, been reported, so that the malignant possibility is to be considered (Luce,⁴ Ross⁵). The variety composed of columnar cells seems to be considered the malignant kind, but the data is inconclusive.

We have been able to follow three patients for periods of two years, one year and nine months respectively. All are well. The first patient had a tumor of the columnar-cell type (No. XVII). Kelly followed a patient for nine years and found he had been in poor health, having had sharp pains in his right iliac fossa and tenderness

² MacCarty, W. C., and McGrath, B. F.: Clinical and Pathological Significance of Obliteration, Carcinoma and Diverticula of the Appendix, *Surg., Gyn. and Obst.*, 1911, xii, 211.

³ Rogg, F. A.: Carcinoma und Carcinoid der Appendix, *Ztschr. f. Krebsforsch.*, 1913, xiii, 12.

⁴ Luce, G.: Ueber sog. primäre Carcinome und primäre carcinome des Wurmfortsatzes, *Beitr. z. klin. Chir.*, 1912, lxxxii, 155.

⁵ Ross, G. G.: Carcinoma of the Appendix, *Philadelphia Tr. Acad. Surg.*, 1912, xiv, 90.

in the incision at all times. This patient had a small-cell carcinoma (No. II in our series). No mention was made of extension or of enlarged lymph nodes in the operative notes in any of the cases.

Diagnosis. In none of our cases was the diagnosis made clinically, in agreement with the reported cases. The diagnosis of acute appendicitis was made in 8 cases, of chronic appendicitis in 4 and the appendix was removed incidental to laparotomy for some other trouble in 5 cases.

Types. The small-cell type occurred in 14 cases, or about 82 per cent., the columnar-cell type in 3 cases, in close agreement with the previously reported cases.

Gross Diagnosis. The tumor was diagnosed grossly in 4 cases. In 4 it could not be recognized grossly even when the histology was at hand.

Situation. Practically all of the tumors were situated at the tip or in the distal third. A bulbous tip was exhibited by four.

Concretions. Concretions were found in two.

Inflammation. Acute inflammation was present in 7 cases, chronic inflammation in 3, an acute exacerbation of a chronic process in 2, obliteration from fibrous tissue in 3 cases. The percentage of these is also in harmony with the previously reported case.

CONCLUSIONS. Three facts stand out very conspicuously in the study of the literature of this neoplasm. Our experience fortified these facts and the practical conclusions which have been drawn are substantiated. The condition has never been diagnosed clinically and a consideration of the symptoms which have been presented by the patients in whom the lesion has been found shows that nothing in any way suggestive of anything other than an ordinary acute or chronic appendicitis is presented. The second fact to be remembered is that the condition may give rise to extension and metastasis. The third consideration is that the condition may be present and yet not be evident on gross inspection either when the appendix is *in situ* or when it is in the pathological laboratory.

It follows therefore that aside from symptoms which lead to its removal it should be removed whenever the abdomen is opened in its neighborhood, regardless of symptoms, for in many cases discovered no symptoms at all were given. Every appendix should be subjected to both careful gross and histological examination.

REFERENCES.

- For further description of cases and literature the following may be consulted:
 Elting, A. W.: Primary Carcinoma of the Vermiform Appendix, with a Report of Three Cases, *Ann. Surg.*, 1903, xxxvii, 549.
 Harte, R. M.: Primary Carcinoma and Sarcoma of Appendix Vermiformis, *Ann. Surg.*, 1908, xlvii, 968.
 McWilliams, C. A.: Primary Carcinoma of the Vermiform Appendix, *AM. JOUR. MED. SC.*, 1908 cxxxv, 822.
 Meyer, L. B.: Primary Carcinoma of the Appendix, *Surg., Gyn. and Obst.*, 1915, xxi, 354.

TWO CASES OF SUPRARENAL DISEASE.

BY OLIVER T. OSBORNE, M.D.,

PROFESSOR OF THERAPEUTICS, YALE UNIVERSITY, NEW HAVEN, CONNECTICUT.

It is not purposed to describe suprarenal disturbances or to discuss the physiology of suprarenal secretion or to discuss the ordinary symptoms of Addison's disease. The following two clinical histories are unique, and for that reason they are presented.

CASE I.—A man, aged thirty-four years, manager of a large factory; not married. He was first seen by me on September 7, 1915. So far as he knew he was well up to February, 1915, when he began to develop brown spots on his face and his whole skin began to darken. This pigmentation increased, spreading down to his neck, over his hands and somewhat over his body, so that at that date, namely, September 7, his face, neck, ears, hands and arms had become as black as the skin of an ordinary negro. The skin of the genitals and the surrounding region was absolutely black. He had a few jet-black pigmented spots on his thighs and some streaks on his back below the neck, with a little lighter (but still darker than normal) skin between these jet-black areas. The sides of his tongue were pigmented black; the top of the tongue was dark. The buccal mucous membrane and the lips were black. In January, 1915, he had weighed 163 pounds; his weight at the date of this examination was 140 pounds. He said he was at times very weak and could hardly move around. His hands and feet became cold and he had to cover himself very warmly at night. He complained of sweating a great deal. Pulse, 96; systolic blood-pressure, 95 mm.; diastolic pressure, 90. The heart sounds were normal but very weak; the lungs were normal; liver somewhat enlarged; right kidney movable and slightly loosened; spleen somewhat enlarged. The urine was normal. Wassermann test and blood examination both had been done in New York; the Wassermann test was reported negative and the blood reported normal.

The previous history showed that this man had never been really sick, except that he had had quinsy the year before. He passed an examination for insurance six years before. He stated that when he was a child his hair was blond, that it turned dark brown at seven or eight years of age, and at this time, September 7, 1915, it was jet black. He stated that his eyes were blue when he was young, then turned brown, and now at this date they were dark brown and the sclerotics were dark and pigmented. His digestion had been good, except that occasionally he had some flatulence; there was no pyrosis, nausea or vomiting. He had never raised any blood nor had a hemorrhage anywhere. He had never had a colic nor any jaundice,

with obstruction of bile passage, and, so far as he knew, he had never passed dark urine.

He had always been a hard smoker, smoking from twelve to fourteen cigars a day. He had never used much alcohol, but he was now taking five cups of coffee a day on account of the bracing effect.

His father died at fifty-nine years of diabetes; his mother died at fifty-eight of some heart trouble. Three brothers and three sisters were alive and well. Several brothers and sisters died very young.

I diagnosed suprarenal disease and gave him a 3-grain suprarenal tablet, three times a day, and a pituitary tablet, each representing 1 grain of the whole gland, twice a day, the latter with the idea of stimulating suprarenal activity.

I next saw this patient on September 14, one week later. The pigmentation had very much diminished from the trunk, leaving only a few darkened areas; the same was true of the mucous membrane of the mouth. The face was not as dark and the insides of his hands were almost normal in color. The amount of urine had been increased. The systolic blood-pressure was 100 and the diastolic 70. The pulse was 84 and very weak. His weight had increased to 138 pounds. His appetite, however, had become poor, and he had a great deal of indigestion, with pain in his upper abdomen, general, not localized anywhere. This pain came on more especially at night and was worse on lying down. He had never had this before. He also had some palpitation of the heart at these times. With this pain his face flushed. He also was having some pain along the spine.

I reduced the suprarenal tablets to two a day and the pituitary substance to one tablet a day.

This patient lived in New York, and the following week he wrote me that his face, hands and body had lost a great deal of the pigmentation, but that he was so weak he could not travel. I did not hear from him again until I learned that he had died on October 19, and an autopsy showed that both suprarenal glands were completely destroyed with tuberculosis and that there were large deposits of calcareous substance in them.

COMMENT. This case is unusual because of the marked symptoms of insufficiency of the adrenal glands, as shown by the unusual amount of pigmentation and the exceedingly low blood-pressure. There was no history of fever. The lungs and other parts of the body were not involved in the tuberculous process. There were no digestive symptoms until the last few weeks of his life. He died from the extreme weakness of his heart and the low blood-pressure. The pulse-pressure was one of the shortest that I have ever noted, the difference between the systolic and the diastolic being, at the first observation, only five points. Under suprarenal it temporarily increased to thirty points.

CASE II.—This patient is a married man, aged twenty-five years, and works in a weaving mill. He was first seen by me in consultation on June 28, 1917, with the history of having been well until May, 1917, when he began to vomit, associated with some cough. He had more or less continued fever, and an eruption of reddish spots on his skin, erythematous in type, this particularly on the feet, arms and elbows, on the flexor surfaces. He also had a great deal of pain in his feet and shoulders and burning sensations and paresthesias of all kinds and tinglings. These disturbances were sufficient to prevent sleep; these spots were not purpuric. There was no hemorrhage, although the gums bled slightly, and he had had several attacks of nose-bleed. His fever ranged about 100° and his pulse was about 100. He could eat practically nothing without vomiting; even water was vomited. He was too weak to stand on his feet. These erythematous and punctate spots disappeared, followed by a little desquamation in these regions, especially on the sides of the fingers and sides of the toes, but scarlet fever, although considered, was decided not to have been present. From this time, namely, about the latter part of May, the discoloration began to increase, and at this date, June 28, 1917, he was on many parts of the body as dark as a colored person, especially on his chest and abdomen, with a few white streaks mixed in with the dark pigmentation. His arms were dark; his face showed dark pigmented spots. At this time his cough had ceased and his vomiting was less frequent, but he was excessively weak and complained of numbness and tingling of his hands and feet from poor circulation. There were no edemas. The urine was negative. He had had very little pain in his abdomen except while vomiting.

This man had never previously been sick. He was married and had three children, the oldest five years of age and the youngest five months, all well. His father was well at seventy-three years; his mother died at sixty-nine years, cause unknown. Three brothers and four sisters were all well.

The heart and lungs were normal. Systolic blood-pressure was 100 and diastolic pressure 60. No history and no signs or symptoms or stigmata of syphilis. He had some pigmented spots in his mouth. The liver was slightly enlarged and the spleen palpable; the rest of the abdomen was negative. His usual weight was 138 pounds; at this date it was 110 pounds. He had a mass of enlarged glands on the left side of his neck, which had been increasing in size. Examination of the blood showed nothing specially abnormal.

A diagnosis of suprarenal disease, probably tuberculous, was made. He was given a suprarenal tablet, three times a day, and iron.

In two weeks the pigmentations began to disappear, and instead of being black on his abdomen and arms he was mottled. The glands of the side of his neck were smaller. There was no diarrhea; he could eat well and retain his food, but he felt very weak and

continued some afternoon temperature. Blood-pressure, 98 mm. systolic and 70 diastolic.

This man was then sent to the Gaylord Farm Tuberculosis Hospital for tuberculin tests. Roentgen-ray investigations of his chest showed no tuberculosis of the lungs; he reacted positively to tuberculin, but there were developed no focal reactions in the lungs. He remained at this hospital for four weeks, gained twenty pounds in weight and under suprarenal treatment the pigmentation almost entirely disappeared.

I saw him again on September 23, 1917, when the only pigmentation remaining was a small amount on the lower back and buttocks. He was running no temperature. The blood-pressure was 110 systolic and 80 diastolic. The tongue was clean; the liver and spleen seemed normal; the urine was negative; he was very weak and unsteady when he walked. The glands of the left side of the neck had broken down and now had formed an abscess. Have advised that his neck be treated surgically immediately. Suprarenal tablets were continued.

COMMENT. I have not seen or heard from this patient since this last date, September 23. I believe the prognosis to be bad in spite of the improvement. The amount of improvement is certainly unusual, especially as to gain in weight.

This case of adrenal disease is again one that is unusually marked by the pigmentation deposits and unusually interesting because of the disappearance of the pigmentation under suprarenal treatment. The loss of muscular strength in both these patients, due to suprarenal deficiency, was very marked. It cannot be entirely attributed to the low blood-pressure, and therefore poor circulation; it is in part, at least, due to muscle weakness.

MAGNESIUM SULPHATE SOLUTIONS IN THE TREATMENT OF SPASTIC CONTRACTURES OF THE RECTUM AND SIGMOID COLON.¹

BY HORACE W. SOPER, M.D.,
ST. LOUIS, MISSOURI.

ONE year ago, Meltzer in the symposium on Gall-stones before the American Gastro-Enterological Association, suggested the employment of a 25 per cent. solution of magnesium sulphate, given through the duodenal tube, in certain obstructions of the common duct, hoping thereby to produce a relaxation of the circular muscle

¹ Read before the American Gastro-enterological Association.

fibers of the ampulla of Vater. The experimental work of Meltzer² demonstrated that solutions of magnesium sulphate produced an inhibitory influence upon the peristaltic movements of the intestinal tract of animals whether the salt was given intravenously or applied directly to the mucosa. Briefly, his hypothesis is that the phenomena of peristalsis consists in a contraction of the proximal and relaxation of the distal part of a section of the intestine, following the law which he designates as "contrary innervation." The purgative action of magnesium sulphate when given by mouth results from the fact that a part of it acts by being converted into sodium sulphate and magnesium carbonate, substances which increase the irritability of the exciting or contractile phase of peristalsis, while the remaining unconverted magnesium sulphate acts by increasing the inhibitory or relaxing phase of peristalsis. From this hypothesis we may deduce that a condition of hypertonus in a section of the intestine is due to a disturbance of the law of contrary innervation, *i. e.*, a preponderance of stimulation occurs in the exciting or contractile phase.

For a long time I have been interested in the muscular contractures which occur in the lower colon and rectum as revealed by sigmoidoscopy. Furthermore, I am convinced that these contractures are pathological in character and that they are etiological factors in many cases of chronic constipation.

The deduction is therefore obvious that solutions of magnesium sulphate applied directly to a hypertonic or contracted segment of the bowel should have the effect of producing a relaxation. In a series of cases I have demonstrated that magnesium sulphate is really capable of overcoming such contractures and that this action may be utilized in the treatment of obstinate constipation.

In a review of 2000 cases of chronic constipation taken from my office files (dating from 1909) the following classification is tabulated.

960 cases of spastic constipation, the spasticities being located in the rectum, sigmoid and descending colon.

210 cases in which the entire colon appeared to be in a state of hypertonic contracture.

403 cases of chronic atonic constipation.

424 cases recorded as "indeterminate," meaning thereby that neither contractures nor atonic conditions could be ascribed as etiological factors.

Cases of partial intestinal obstruction due to organic conditions, such as strictures, growths, inflammatory processes, etc., are not included in the above series.

The proctosigmoidoscope is the most valuable diagnostic agent in the detection of hypertonic contractures.

² The Relation of the Purgative Action of Magnesium Sulphate to Peristalsis and the General Law of Crossed Innervation, Arch. Int. Med., June, 1915, No. 6, xv, 955.

No one experienced in its use will doubt the existence of the spastic form of constipation.

In cases in which the contracture is beyond the reach of the sigmoidoscope the diagnosis is made by the subjective symptoms, the characteristic fragmentary feces, combined with a strongly contracted palpably tender descending colon.

The x-ray diagnosis of contractures is extremely unreliable, chiefly because of the position and form of the sigmoid colon. The bismuth or barium enema will pass through an organic or spasmodic stenosis whose lumen is of very small caliber. It may canalize contracted areas which are concealed by the distended portion of the bowel and thus escape detection, especially as palpation is practically impossible in this region. Moreover, the bismuth or barium meal given by mouth is frequently scattered in a thin column along the lower colon giving an impression of contracture when no narrowing exists. Also the degree of tonus frequently changes in the normal colon and interpretation presents extreme difficulties. The illustrations show the difficulties encountered in attempting to make roentgenoscopic diagnoses of contractures.



FIG. 1.—A case of strong contracture at the rectosigmoid angle, but not visible in the plate.

Contractures of the rectum and sigmoid vary in intensity from mild contractures which readily yield to dilatation to strong spasms which form unyielding obstruction. The contractures may be located at any point in the rectum, sigmoid, colon, or descending colon including the splenic flexure. The most frequent site is

the rectosigmoid junction. Severe contractures at this point present a syndrome which I³ have designated "sigmoidospasm."



FIG. 2.—The sigmoidoscope reveals strong contracture involving the first four inches of the sigmoid. The contracture is not visible in the plate.

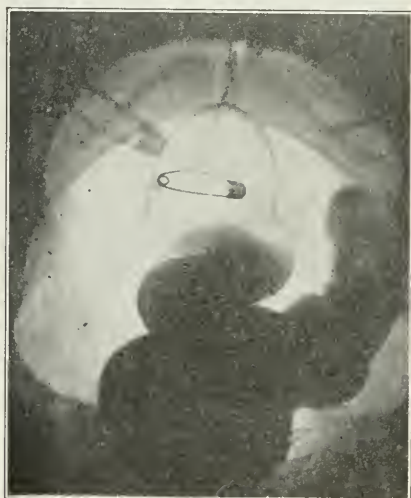


FIG. 3.—This case is one of atony of the rectum and sigmoid. The atonic condition is well shown in the plate.

An obstinate form of constipation results from combined contractures and dilatations, *e. g.*, (*a*) atony of the rectum and sigmoid

³ Soper, H. W.: Sigmoidoscopy, *Internat. Clinics*, 1916, iv, 260.

associated with contracture at descending colon; (b) contraction at rectosigmoid angle and atony of sigmoid loop; (c) contracture at splenic flexure and descending colon and atony of cecum.



FIG. 4.—Shows an apparent contracture. However, sigmoidoscopy revealed a perfectly normal condition.



FIG. 5.—Shows an apparent contracture. Yet sigmoidoscopy revealed perfectly normal condition.

ACTION OF MAGNESIUM SULPHATE APPLIED DIRECTLY TO CONTRACTURES. OBSERVATION MADE UPON 220 CASES. 1. A saturated solution was found to be most efficient.

2. The solution was applied by means of cotton applicators through the sigmoidoscopic tube (knee-chest position). A char-

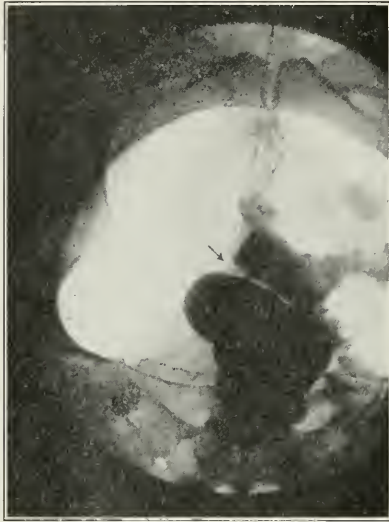


FIG. 6.—This is a case of strong, obstinate contracture at the rectosigmoid junction, possibly shown in the plate.

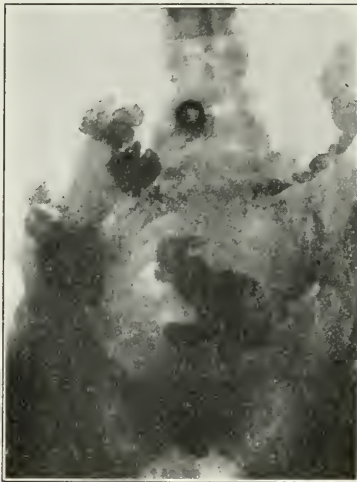


FIG. 7.—This is an obstinate case of constipation with spasticity of the entire colon and rectum.

acteristic diffuse, deep pink color of the mucosa is observed within from ten to twenty seconds.

3. Mild contractures disappear within a few seconds. Moderate contractures require a minute or two. Strong spasms require a series of applications to produce relaxation.



FIG. 8.—Shows a contracted and distorted sigmoid due to chronic adhesive perisigmoiditis. The picture is in accord with the sigmoidoscopic findings.

TREATMENT OF CONSTIPATION EXCLUSIVELY BY SATURATED SOLUTIONS OF MAGNESIUM SULPHATE. Eighty obstinate cases which had been under my care for a year or more. They had been under treatment by dietetic measures, enemata of oil, agar-agar, dilatations by means of oil applicators, insufflations of air, etc. None of them had been able to get along without the use of the oil enema. Sixty-eight cases have apparently been completely restored to a condition of normal colonic function. The number of treatments required in these cases varied from ten to thirty applications given every second or third day.

Five cases were complicated by inflammatory induration and distortion of the bowel at the rectosigmoid junction, consequently treatment was ineffectual.

In 7 cases the contractures were overcome but normal colonic function was not restored.

Seventy-two new cases of obstinate spastic constipation, *i. e.*, cases that were of long standing but that had not been previously under my care. Sixty-four cases were successfully treated with satisfactory restoration of bowel function. Eight cases were extremely neurotic individuals who could not stand the treatment although no real pain is produced by it.

Sixty-eight cases of obstinate spastic constipation, cases of long-standing constipation, but which presented contractures that were moderate in character, *i. e.*, that readily responded to treatment

and required but from six to ten applications to restore good colonic function.

The plan usually adopted is for the patient to return for treatment every second day, gradually lengthening the interval between treatments as the bowel function is restored. Purgatives and enemata of water must be avoided, inasmuch as they both increase the tendency to contraction. Oil enemata may be used in conjunction with the magnesium sulphate treatment when it is not convenient for the patient to come to the office for frequent treatments.

Cases in which the contracture is beyond the reach of the sigmoidoscope are treated by passing a soft-rubber catheter through the sigmoid tube and injecting 2 ounces of the magnesium sulphate solution, the patient retaining the knee-chest position for several minutes thereafter.

Sigmoidoscopic examinations of patients in whom normal function had been restored revealed the absence of previously demonstrated spastic obstructions.

While it is too early to assert that these patients are permanently cured, nevertheless some of the most obstinate cases have remained in a satisfactory condition for more than ten months.

THE ACTION OF ENEMATA OF MAGNESIUM SULPHATE IN THE RELIEF OF POSTOPERATIVE ABDOMINAL DISTENTIONS AND GAS PAINS. Observations of the condition presented by postoperative abdominal distention suggested the use of magnesium sulphate enema as means of relief. Roentgen-ray examination of 6 cases revealed that the colon alone was involved, no gas being found in the small intestine. The rectum and lower sigmoid were free from gas. Sigmoidoscopic examination showed the presence of marked contractures in the rectum and lower sigmoid. In a series of 30 cases I used an enema of saturated solution of magnesium sulphate given through the rectal tube. The technic is as follows:

Three ounces of saturated solution of magnesium sulphate is introduced by means of the rectal tube passed 4 or 5 inches into the bowel, elevating the hips whenever possible, and having it retained as long as possible. This procedure may be repeated every day, or several times a day if so desired.

The effect was quite remarkable. Large quantities of flatus were expelled, followed by immediate relief in 24 of the cases. The enema is usually retained for not more than five minutes. Occasionally it is retained for twenty-four hours; however, no harm results as no toxic effects have been noted.⁴ Defecation often follows, not characteristic of a purgative dejection, but should the colon happen to contain much fecal matter, many passages may result. No rectal pain nor tenesmus follows the daily use of the

⁴ Meltzer warns against giving too large a dose, as toxic effects have been observed particularly in animal experimentation.

enema. No evidence of increased peristalsis occurs. The magnesium sulphate solution evidently merely relaxes the contracted rectum and lower sigmoid and permits the retained gases and fecal matter to pass out of the distended colon.

The enema was also used in 2 cases of partial obstruction of the lower colon and sigmoid with very beneficial results. One such case was seen in consultation with Dr. H. G. Mudd. Patient, female, aged seventy-five years, presented the clinical picture of acute intestinal obstruction with great distention of the abdomen and much pain. Operative intervention was seriously considered. Patient had previously received large doses of cathartics, enemata of water, etc., without effect. The magnesium sulphate enema repeated from time to time was very effective. A later study of the case revealed that an adhesive periproctitis had resulted in a partial obstruction in the upper rectum. Evidently a muscular spasm was partly responsible for the stenosis which was overcome by the magnesium sulphate.

A second case was seen in consultation with Dr. John R. Caulk. The obstruction was located in the sigmoid loop, due to an extension of a pelvic abscess. Magnesium sulphate was again very effective, the patient making a good recovery. Within a week the operation of prostatectomy was successfully performed.

Realizing that personal enthusiasm is apt to impair one's judgment in forming an opinion as to the value of a therapeutic procedure, I asked several surgeons to try the enema in cases of postoperative gas pains and report their results to me. The replies representing 222 cases are summarized as follows:

Dr. Francis Reder: Magnesium sulphate inferior to alum enema combined with pituitrin.

Dr. W. H. Vogt: Magnesium sulphate inferior to intramuscular injection of pituitrin.

Dr. N. B. Carson: Used dilute solutions and results not satisfactory.

Dr. Mary H. McLean: Favorably impressed.

Dr. V. P. Blair: Favorably impressed.

Dr. Ernest Jonas: Favorably impressed.

Dr. G. D. Royston: Favorably impressed.

Dr. Willard Bartlett: Treatment of great value.

Dr. E. J. Neville: Treatment of great value.

Dr. O. H. Elbrecht: Treatment of great value.

Dr. John McH. Dean: Treatment of great value.

Dr. John R. Caulk: Treatment of great value.

Dr. H. G. Mudd: Treatment of great value.

Dr. P. Y. Tupper: Treatment of great value.

Dr. H. L. Nietert: Used it for years, and finds it of great value.

Dr. Major G. Seelig: Used it successfully for years in 50 per cent. solution combined with turpentine and green soap.

Dr. Tupper thus describes its effect: "Within a short time, ordinarily within one-half hour, there has been a free passage of flatus accompanied, not infrequently, with a fecal evacuation. Apparently the salt acts directly upon the rectum and lower sigmoid, causing relaxation of the muscular coat without producing peristalsis of either the large or the small intestine. Because of this the therapeutic measure is safe and especially serviceable soon after operations upon the intestine where evacuation of flatus is necessary for the patient's comfort and safety and where active peristalsis might produce serious results.

"Magnesium sulphate thus applied apparently is more effective than the enemata ordinarily used and is apparently free from the discomfort and danger accompanying their use."

I wish to express my thanks to Dr. R. Walter Mills for the roentgen-ray work and to Dr. D. L. Penney for valuable aid in the treatment of the cases.

CONCLUSIONS. 1. Spastic contractures of the lower colon are etiological factors in many cases of chronic constipation.

2. These contractures are the result of disturbances in Meltzer's law of contrary innervation.

3. A saturated solution of magnesium sulphate applied locally to the contracted segment produces a relaxation. Repeated applications finally overcome the spasticity and permit the restoration of normal colonic function.

4. Contractures in the rectum and lower sigmoid, with accompanying dilatation of the colon, are found in many cases of post-operative abdominal distention. Magnesium sulphate enemata are very efficacious in relaxing the contractures and thereby relieving the distention and "gas pains."

5. Enemata of magnesium sulphate are also very useful in partial organic obstructions in the rectum and lower colon, inasmuch as they relax accompanying muscular contractures without stimulating peristalsis.

6. Magnesium sulphate solution applied by means of the cotton applicator greatly facilitates the introduction of the sigmoidoscope.

SARCOMA OF THE HEART.

BY I. PERLSTEIN, M.D.,

CHICAGO, ILLINOIS

(From the Pathological Laboratory of the Michael Reese Hospital and the Nelson Morris Memorial Institute for Medical Research, Chicago Illinois.)

INTRODUCTION. Of the various organs of the body the heart is the least frequent site of primary neoplastic change. Tumors of

the heart are therefore of pathological interest because of their rarity. They should excite a certain degree of clinical interest because there arises the question of the possibility of making a clinical diagnosis of cardiac tumor. As a matter of fact, tumor of the heart has never been diagnosed, *intra vitam*, as is apparent from a review of the literature of the subject.

Primary tumors of the heart are of less frequent occurrence than secondary tumors. The latter most often reach the heart by direct contiguity from tumors of the mediastinum and from tumors of the lungs, of the pleura, of the sternum, of the stomach, etc. They may also be carried to the heart from some distant organ, but this occurs infrequently. Metastases in the heart have been reported from malignant growths occurring in practically any part of the body, as cancer of the breast, of the stomach, penis, uterus, of melanotic sarcoma of the eye, etc. Tumors of the adrenals have been found to reach the heart by progressive sarcomatous thrombosis. Secondary tumors are more often carcinomas than sarcomas.

The first who called attention to the presence of a tumor of the heart, according to Tedeschi,¹ was Theophy Boneti, who found such a tumor, together with marked edema of the lungs, as reported in *Sepulchretum sivi anatomia practica ex cadaveribus morbo donatis*, Geneva, 1700, JIII, Miscellanea, p. 505. Morgagni, in 1762, described numerous polypoid formations in the heart. (*De sedibus et causis morborum*, etc. Epist. XVI, Napoli, 1762.) We have no criterion as to the exact nature of the tumors described by these older writers. We do not know whether they were real blastomas or only blood-clots and organized thrombi, but we have to consider the possibility that they may have been real neoplasms.

The first authentic report of a primary cardiac tumor is that of Albers, who reported a primary cardiac "chondroid" in 1835, and later²⁷ corrected his diagnosis according to the progress which had been made in pathology, and called it a fibroma. The first sarcoma was reported by Bodenheimer in 1865. In looking over the literature one finds that more than 100 cases of primary tumors of the heart have been reported, but many of these must be rejected because they are not true tumors or are not primary in the heart.

Tedeschi,¹ reviewing the literature on this subject, counted up 86 cases, including 3 of his own. Unquestionably many of these cases are secondary tumors. Berthenson² found only 30 cases of unquestionable primary tumors, and his resumé dates from the same year. Among these 30 tumors were 7 sarcomas. Link³ was able to collect 91 cases, but only 23 were of value from a clinical point of view. In his list are 13 sarcomas. Ehrenberg⁴ collected 19 cases of sarcoma of the heart.

Among 2942 autopsies performed at the Johns Hopkins Hospital were found 10 heart tumors. These were all secondary except one rhabdomyoma. They were 1 sarcoma, 1 lymphosarcoma, 2 epithe-

liomas, 1 endothelioma, and 4 carcinomas (Bryant).⁵ From 1903 to 1907 there were 6655 autopsies performed at the Pathological Institute of the University of Berlin. Among these were found 15 secondary carcinomas of the heart and 4 secondary sarcomas (Karrenstein).⁶

Many of the older writers report cancers of the heart. Indeed, it appears as if they called any malignant growth of the heart a cancer. These reports date back mostly to the premicroscopic days, and they are of little value to us from a pathological point of view. A carcinoma of the heart of a child of three days was reported by Billard in 1828, and Andrale and Boyle in 1824 reported a case of a carcinoma in the wall of the right ventricle (cited from Schöppler).⁷

However, primary carcinomas of the heart have been reported quite recently. Dietrich⁸ reported a growth the size of the palm of a hand on the anterior and right mediastinal surface of the upper part of the pericardium in a woman, aged forty-four years, who died suddenly after having suffered for two months with dyspnea and anxiety without real heart difficulties. This tumor, a papillary carcinoma, did not infiltrate the myocardium, and the author considered it to be a primary carcinoma originating in the parietal pericardium, for no focus was found after careful search in any part of the body. Foerster and Garnieri⁹ also reported a case of primary carcinoma of the pericardium (*Un caso de cancro endotheliale primitivo del pericardio*). It is difficult to understand how a primary epithelial tumor could originate in an organ which does not contain any epithelial tissue, unless the tumor has originated from the covering pericardial mesothelium.

The most common tumors of the heart are fibromas, myxomas, and fibromyxomas. Next in frequency are the sarcomas. Rhabdomyomas, lipomas, angiomas and lymphangiomas also have been reported. A teratoma has been reported by Joel.¹⁰ This tumor was within the pericardial cavity attached to the pulmonary artery where it leaves the heart. Of special interest are the rhabdomyomas. They are a characteristic, well-defined group. Usually they are congenital, and in about 50 per cent. of the cases they are associated with a tuberous sclerosis of the brain.

Of late years the fibromas and the fibromyxomas have attracted special attention. According to several investigators, as Thorel, Stahr and others, many of this class of tumors reported as primary are not genuine blastomas but pseudotumors, namely, organized thrombi which have undergone a certain metamorphosis by edematous changes and formation of elastic fibers. Méroz,¹¹ in 1911, reported 3 primary heart tumors which were found among 3000 autopsies. Two of these he diagnosed as fibro-élastomes hémorrhagiques and the third one as a sarcoma. The first 2 are considered by Thorel as organized thrombi. There is no question but that many of these tumors are nothing but organization tissue.

The origin of these neoplasms may be in any of the layers of the heart wall, in the endocardium, the myocardium or the epicardium. Some of the tumors reported had their origin in the parietal pericardium, but the majority originated in the endocardium. Link,³ in his report of 91 cases of primary tumor, pays special attention to the site of the tumor. He finds that 24 among this number were located in the left auricle, 10 in the right auricle, 14 in the right ventricle and 8 in the left ventricle. Sixteen were valve tumors; 3 were situated in both auricles; 2 in both ventricles; 2 in the right auricle and ventricle; 2 in the left auricle and ventricle; 2 only in the auricular septum.

According to the type of cell of which they are composed, sarcomas of the heart are classified as round-, spindle-, mixed- and giant-cell sarcomas, and with regard to their structure they may be plain sarcomas, myxosarcomas, fibrosarcomas and angiosarcomas. An osteosarcoma and a sarcoma lymphangiecticum have been reported in dogs.

The etiology is of course unknown. Ribbert thinks they may be due to superfluous cell material in the auricular septum due to disturbances in development. The reason for the rare occurrence of cardiac tumors is, according to Adami,¹² that "The heart above all organs is constantly in a state of great efficiency, well nourished, well innervated and functionally always active, so that it is less likely to take on aberrant growth."

Symptoms, Clinical Course and Diagnosis. That a clinical diagnosis of tumor of the heart has never been made can be explained by the fact that this pathological condition does not produce a characteristic picture. The diagnosis, which appears to me the most rational, was the one made by Biermer, who diagnosed the case reported by Bodenheimer¹³ as "cardiac disease of unknown origin."

From a clinical point of view we may divide tumors of the heart into two groups: (1) those which produce symptoms, and (2) those which do not produce symptoms.

Frequently these patients do not present any, or very few, symptoms suggesting cardiac trouble. Some die suddenly and without having shown any signs of the disease, and the cardiac tumor is then found on the autopsy table as a surprise. In some cases the symptoms appear suddenly and death occurs in a short time. The reason for this may be that a malignant growth of the heart may remain stationary for a long time, the same as an ulcer rodens or a carcinoma of the stomach, and then flare up suddenly and produce severe symptoms and death in a short while, as in the author's case.

The symptoms which are produced by a cardiac tumor depend upon its location and upon its size. We may easily understand that a small tumor located on the surface of the heart, not interfering with the circulation, may not produce any symptoms whatsoever. However, a tumor, even if of a very small size, located on or near

a valve, is liable to produce a stenosis of a cardiac orifice or prevent proper closure of the valve, so that soon symptoms of disturbed circulation may arise. When a tumor is large its mere size is apt to produce these symptoms by encroaching upon the cavities of the heart or by pressure upon the large veins. It is evident that these symptoms are produced mechanically. How sudden death may thus be produced is demonstrated by Fuhrman's case. In this case the ostium of the right coronary artery was occluded by a sarcomatous growth, and a sarcomatous embolus was found at the opening of the left coronary artery. In the cases of secondary cardiac tumor, when a focus exists in some part of the body, a metastasis into the heart may sometimes be inferred, when suddenly heart symptoms develop in a previously well-working heart, but even here no certain diagnosis can be made.

As to the diagnosis of cardiac tumors, Hoover¹⁴ states that "it is either impossible or a matter of good fortune." When symptoms are present they are those of heart disease, and the clinician then thinks properly of the more common morbid conditions, "for unless we wish to indulge in the merest guesswork we must hold fast to the principle that in an individual case the probabilities are more in favor of ordinary clinical conditions than of the rarer anomalies."¹⁵

Several writers have tried to find symptoms which are diagnostic of cardiac tumors, but they did not succeed. Bodenheimer¹³ states that "one can think of heart tumor when history, clinical examinations and observation do not speak for any other heart disease, when the symptoms occur rather suddenly and unexpectedly and the condition *soon* takes a faster, *soon* a slower course."

Krehl¹⁵ states that it is suggestive of heart tumor when a marked congestion occurs along the course of one vein, while other parts, which also ought to be affected in the course of ordinary cardiac disease, escape altogether. Fraenkel¹⁶ considers the frequent recurrence of hemorrhagic pericardial effusion, necessitating frequent paracenteses, as a diagnostic symptom of cardiac tumor, and Eichhorst¹⁷ states: "It must be said that tumors of the heart hide themselves sometimes behind the picture of pericarditis." The most important diagnostic means used today are the roentgen-ray picture and the fluoroscope. Only in 2 of the cases reported below (Ehrenberg and Sternberg) were these means used, for most of the cases were reported before we had these means of diagnosis.

REPORT OF CASE. The rare occurrence of primary sarcoma of the heart induces me to report the following case of sarcoma which originated in the subepicardial areolar tissue. It is of interest because of its large size, its well-defined structure and on account of the hemothorax which was associated with it.

The patient, a business man, aged forty-three years, entered the Michael Reese Hospital, December 4, 1916, as a private patient

Since the pleural cavity filled up so fast after each thoracentesis a thin catheter was introduced and left there for drainage after several thoracenteses had been done. Several times air was injected into the pleural cavity after 500 to 1000 c.c. of fluid had been withdrawn.

An intravenous infusion of 60 c.c. of blood was performed on December 15 and of 50 c.c. on December 16.

Examinations of the sputum for tubercle bacilli were made December 6, 11 and 12. The usual organisms were present and no tubercle bacilli were found.

The Wassermann test was made on the blood December 4, 11 and 15, and found negative each time.

A guinea-pig was injected intraperitoneally with the pleural fluid on December 7. It did not develop tuberculosis.

The patient's temperature on admission was 100° F. and never went over 102.4°. The pulse was always over 100. Usually it was between 108 and 120; the highest rate recorded was 130.

In the urine several times a trace of albumin was found and a few epithelial cells or leukocytes.

It is interesting to follow the blood changes with the continual loss of blood:

		Red blood count.				Hemoglobin, per cent.		White count.		
December	4	.	.	.	5,080,000	90		21,800		
"	6	.	.	.	5,696,000	85		20,000		
"	7	.	.	.	5,696,000	..		22,200		
"	8		28,600		
"	10	.	.	.	4,867,000	75		27,800		
"	12	.	.	.	4,013,000	70		26,000		
"	14	.	.	.	3,167,000	50		48,400		
"	15	.	.	.	2,987,000	50		112,000		
"	16		134,000		
"	17	.	.	.	2,203,000	45		122,000		

		Differential count.*							Cells counted.				
		N.	S. M.	L. M.	T.	E.	B.	N.	Stain.	Cells counted.			
December	4	.	.	.	82	12	6	0	0	0	0	Wright	100
"	8	.	.	.	86	9	5	0	0	0	0	"	100
"	17	.	.	.	89	4	7	0	0	0	0	"	100

The coagulation time on December 9 was 3.5 minutes and on December 10, 3 minutes.

The blood-pressure on December 6 was 115, 90 and 25 mm., and on December 7, 110, 85 and 25 mm.

The pulse was intermittent, weak and irregular; respiration was at times irregular, usually over twenty and sometimes as high as forty per minute. The outstanding symptoms were shortness of breath, profuse perspiration, restlessness, vomiting, nausea, dizziness, feeling of faintness, weakness, thirst and coughing. He died December 21, 1916, at 12.05 A.M.

All these symptoms can be explained by an excessive loss of

* N. = Neutrophiles L. M. = Large Mononuclear B. = Basophile
 S. M. = Small Mononuclear T. = Transitional cell N. = Nomoblast
 E. = Eosinophile

blood, which is the outstanding and most remarkable feature of this clinical picture. Altogether 15,350 c.c. of bloody fluid were obtained from December 4 to December 19. A definite diagnosis as to the reason for the continued bloody exudate in the pleural cavity was not made. Since the common symptoms of heart disease, as murmurs, edema, ascites, etc., were not present, tumor of the mediastinum and tuberculosis mainly were thought of. No tubercle bacilli were found in repeated examinations of the sputum and the pleural fluid, and tumor of the mediastinum was left as the probable diagnosis.

REPORT OF AUTOPSY. The postmortem examination was performed ten hours after death. The anatomical diagnosis was as follows: Subepicardial sarcoma of heart (mixed cell). Metastases into pericardial fat, pleura and mediastinal lymph glands. Chronic obliterative pericarditis. Left hemothorax. Patent foramen ovale. Arteriosclerosis of ascending aorta. Adipositas cordis. Atelectasis of left lung. Chronic fibrous pleurisy of right lung. Passive congestion of upper lobes of right lung. Lobar pneumonia of right lower lobe. Anthracosis. Acute and subacute interstitial pneumonia. Chronic emphysema. Acute splenitis. Acute inflammation of adrenal glands. Cloudy swelling of liver, pancreas and kidney.

The body is opened by the usual longitudinal incision. A thick layer of yellow subcutaneous fat is present.

Chest. On opening the thoracic cavity the right lung is found adherent to the chest wall by a moderate number of old dense adhesions. The left pleural cavity contains about one liter of bloody fluid. The left lung is very small, occupying the lower and posterior part of the left pleural cavity. The heart and the space between the lungs are covered with an unusually large amount of fat. The parietal and visceral pleura on the left side are thickened and covered with a soft, jelly-like, mushy or stringy, grayish exudate which is covered with blood, giving the parietal wall, especially on its left lateral and posterior aspect, a ragged appearance. The left lung is adherent to the chest wall by this material, but is easily loosened.

The left pleura presents on its visceral surface many grayish-white, irregular areas of different size, measuring up to 7 cm. in diameter. They are not raised from the surface of the pleura. On cross-section they are not seen to invade the lung tissue. They are 1 to 2 mm. thick.

Lungs. The small left lung is entirely submerged in bloody fluid and is not seen when the chest is opened. It weighs 287 grams. Adhesions of the character described above are present between the lower lobe and the diaphragm, between the lung and the mediastinum, and between the lung and the chest wall. Its color is red like that of muscle, on the surface as well as on cross-section. It is firm to touch, crepitus is absent and pieces excised sink in water.

The right lung weighs 555 grams. Isolated, old, dense adhesions

are present between the lung and the parietal wall. The adhesions are marked between the right lower lobe and the diaphragm; in loosening them the lung tissue is torn. Under the pleura many blackish areas of different size are seen (an̄thracosis). On section the upper lobe is crepitant, but is dark red and congested. Excised pieces float on water. From the cut surfaces a bloody, frothy fluid escapes. The lower lobe is of increased firmness; crepitus is present, but greatly diminished. On cross-section it is dark red in color and a bloody fluid, with some air bubbles in it, escapes on pressure. Excised pieces sink in water. No tumor metastases are seen or felt in the lung tissue.

Heart. The heart is hidden in an unusually large mass of lobulated, yellow fat, which is somewhat firmer than usual. The amount is so large that on first inspection the heart is not seen at all. The pericardial sac is completely obliterated, the parietal and visceral layers of the pericardium being firmly adherent to each other. On the left border of the heart a tumor is present. On account of the large amount of fat around the heart its borders and size cannot be made out. The tumor tissue is cystic in the incised area. A slightly cloudy fluid escapes from the incised cysts. One area in the center is broken down and a bloody and pus-like fluid escapes from it. The heart, with its vessels entering and leaving at the base, the right lung, the trachea and its bifurcating bronchi are removed *in toto* and dissected after having been hardened in formalin. From the hardened specimen the fat is removed and the tumor is found occupying the right border and the larger part of the posterior and the diaphragmatic surface of the heart. The lower border of the tumor is 5 cm. from the apex. The superior pole reaches up to the pulmonary artery, which arches over it (Fig. 1, *c*). The entire tumor in its largest diameters is 13 cm. long, 8 cm. wide and 5 cm. thick. The ascending aorta is anterior and to the right of its upper part. The left auricle is to the right of it and both ventricles are anterior to the lower part of the tumor. The lower surface which rests against the diaphragm measures 6 by 6 cm. This surface presents a ragged appearance after having been loosened from the diaphragm, due to the adhesions which have been broken up here.

The tumor consists of two portions (Fig. 1, *d*), a lower which forms part of a sphere and an upper one which is cone-shaped. Between these two portions is a constriction (Fig. 1, *e*). The lower part is the larger and projects from the surface of the heart, on which it rests by a large base.

On incising the tumor it is found to be sharply outlined. It is covered with pericardium. The latter is moderately thickened and its external surface is roughened. It is seen to consist of two layers which in most places can be easily separated. The tumor can be shelled out from this membrane like an orange from its peeling. (Fig. 1, *g*). In some places, especially in the inferior part of the tumor, the pericardial membrane is more firmly adherent to it.

The surface of the tumor, exposed under the pericardium, is smooth and of a white color. The line of demarcation of the tumor and the myocardium is also well defined, and the tumor tissue is differentiated from the myocardium by its color, consistency and general appearance. The color on cross-section is grayish-white. In some places it is soft in consistency and fat-like to touch in the fresh specimen; in other areas it is firmer. The cystic portion feels cartilage-like in the hardened specimen. These cystic cavities, which are present only in the lower part of the tumor (Fig. 2), are of

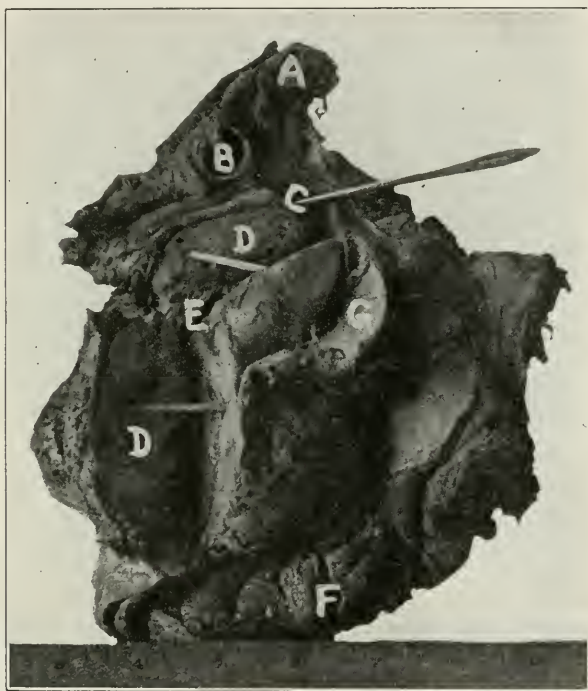


FIG. 1.—Photograph of posterior aspect of heart. A, trachea; B, bronchus; C, probe in pulmonary artery; D, the two lobes of the tumor with a constriction at E; the tumor is incised and the two halves pried apart by two pieces of wood; F, wall of left ventricle; G, the two layers of the pericardium peeled off from the tumor and reflected.

variable size and shape and measure up to 1 cm. in diameter. In the center of the lower as well as in the upper portion are brownish-red areas of degeneration. They are most marked in the lower part, where one cavity is present, about 2 cm. in diameter, containing bloody, purulent fluid. The upper portion produces a bulging into the wall of the aorta, but leaves enough free space here to allow the circulation of the blood. No metastases are seen in the veins at the base of the heart. The myocardium is normal in color and general appearance. The wall of the left ventricle is 12 mm. thick. It is nowhere seen to be invaded by the tumor tissue,

The endocardium is smooth and glistening. No tumor masses are present on it. The valves are smooth and competent. Only the aortic valve presents a slight thickening at the bases of the cusps.

Some yellowish, hardened patches are also seen in the ascending aorta.

The foramen ovale is closed except for a slit-like opening at the upper border of the fossa ovalis, but the layers of the endocardium are overlapping here, preventing the blood from flowing from the right auricle into the left.

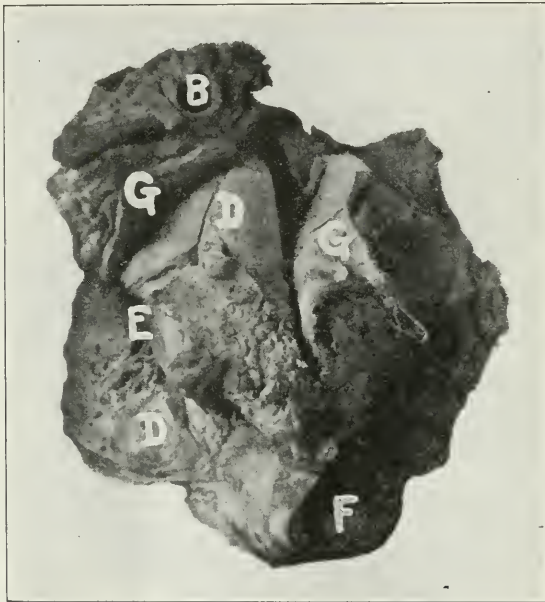


FIG. 2.—Shows the cystic degeneration of the lower part of the tumor which is laid open. *B*, bronchus; *D*, the lobes of the tumor, with a constriction at *E*; *F*, wall of left ventricle; *G*, the two layers of the pericardium peeled off from the tumor and reflected. This figure shows the cystic degeneration in the lower portion of the tumor.

The glands at the roots of the lung and in the mediastinum are not increased in size or number. The largest glands are about the size of a bean, and on macroscopic examination they were not considered to contain metastases.

The examination of the abdomen did not show anything of special interest. A large amount of fat was present on the large intestine, in the mesentery and retroperitoneally. There was no fluid in the abdomen. The abdominal organs appeared anemic. The liver tissue was of a yellowish color, suggesting fatty changes. It weighed 2170 grams. The spleen weighed 100 grams and appeared somewhat firmer than usual. The kidneys were pale and cloudy and weighed 200 and 190 grams respectively. The intestines were very anemic; pancreas, bladder, adrenals and prostate appeared normal. A

thorough examination for a focus of tumor tissue in any other part of the body was made and no focus was found.

Microscopic Report. Heart. Sections from different parts of the tumor were examined. One section shows the relation of the myocardium and pericardium to the tumor. It is taken from a place where myocardium, pericardium and tumor tissue meet. A large portion of this section consists of myocardial muscle, which is cloudy and infiltrated by lymphocytes and pus cells. Some of the nuclei of the myocardial muscle are rather large and deeply stained.

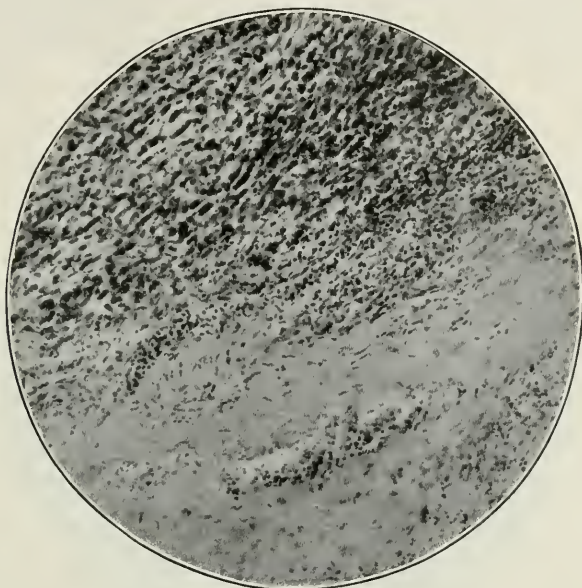


FIG. 3.—Photomicrograph of a section which is taken from the border of the tumor and includes a portion of the pericardium. There is a marked infiltration of small round cells, especially in the pericardium. Mayer's hemalum and eosin. Magnification, 140.

Next to the heart muscle is a layer of subepicardial fat, infiltrated by pus cells and lymphocytes. Peripheral to this is a zone consisting of fibrous tissue. In part of the section this layer is deflected. Here, next to the subepicardial fat, is tumor tissue, and the layer of fibrous epicardium and pericardium runs along the outer border of the tumor, so that the latter is bordered by pericardium on the one side and subepicardial fat on the other. Pericardial fat is peripheral to the pericardium, and it is richly infiltrated with tumor cells.

The pericardial tissue covering the myocardium and the tumor is diffusely infiltrated with large numbers of lymphocytes and a moderate number of pus cells. It contains many young small bloodvessels and cellular strands, consisting of spindle cells and lymphocytes. The connective tissue next to the tumor is hyaline-like and contains few nuclei (Fig. 3). In one area there is a small

number of tumor cells in the pericardial connective tissue. Between the tumor and the pericardial connective tissue are large masses of lymphocytes. The tumor is made up of closely packed cells which are mostly oval, round or spindle shaped (Fig. 4). Their size varies, but most of them are rather large. Their nuclei are prominent, rich in chromatin and stained deeply blue. Abnormal mitotic figures are present. Most of the spindle-shaped nuclei have fibrillar protoplasm on both poles; around the round cells little or none is seen. The connective tissue is small in amount and the blood supply is poor. Large areas of the tumor tissue are necrotic. These areas are stained well with eosin, have a homogeneous appearance and

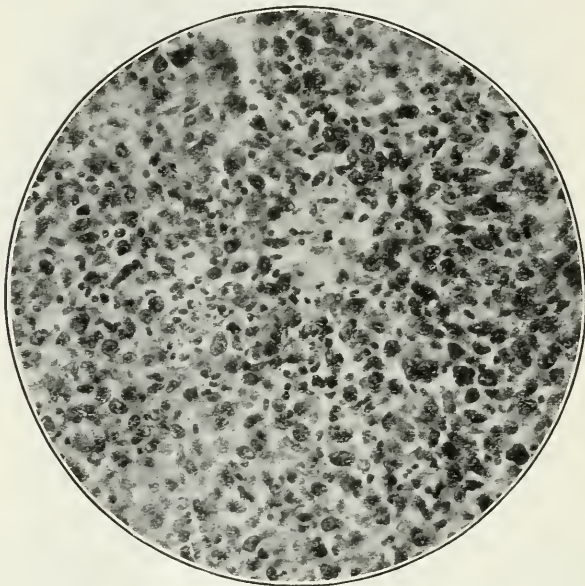


FIG. 4.—Photomicrograph of a section of the tumor showing the type of cells and the structure. Mayer's hemalum and eosin. Magnification, 285.

contain much pyknotic nuclear material. The tumor tissue in this section and all the other sections examined is richly infiltrated with pus cells and lymphocytes.

A section taken from the cystic area presents mostly necrotic tumor tissue. The cyst wall consists of necrotic tissue without nuclei. The cavity contains chiefly pus cells and red blood corpuscles. Large areas of pyknosis are present, and other areas, which are stained deeply with eosin, contain no nuclei.

In a section from that part of the tumor which rests against the diaphragm four zones are present. The first zone consists of tumor tissue, which is largely necrotic. The pericardial layer next to this divides and encloses a large area of tumor tissue, which appears to

be in the obliterated pericardial cavity. Peripheral to this is the pericardial adipose connective tissue, richly infiltrated with tumor cells, and outside of this is necrotic sarcomatous tissue. The irregular torn adhesions of the diaphragmatic surface of the tumor are made up of sarcomatous tissue according to this section.

Myocardium. The surface of this section consists of a dense connective tissue, which is infiltrated by numerous lymphocytes and pus cells. In some regions two layers can be recognized, separated by fibrin and inflammatory exudate. These two layers correspond to the parietal and visceral epicardium and are fused together by inflammatory tissue. Beneath this layer is the subepicardial fat. The myocardial muscle contains moderate numbers of lymphocytes and leukocytes, especially in the bloodvessels. The cardiac muscle cells are cloudy. In one area this condition is pronounced, the muscle appears opaque and homogeneous and in some fibers the nuclei appear to be lost. No metastases were found in the myocardium in this section nor in any of the other sections which were examined.

Lung. Numerous leukocytes and lymphocytes are scattered throughout the sections. They are contained chiefly in the connective tissue of the alveolar septa and in the small bloodvessels. The alveoli contain air; some are distended and the septa between the alveoli are thinned or broken in places. Some of the air sacs contain serum with desquamated epithelial cells and a few leukocytes and lymphocytes.

In a section from the left lung taken from one of the grayish areas described in the gross examination the lung is covered by a thick layer of sarcomatous tissue. Peripheral to this is a thin layer of connective tissue, infiltrated with lymphocytes and containing numerous spindle nuclei and some leukocytes. The tumor cells are large and prominent, rich in chromatin, and appear to be younger than in the original tumor. No areas of degeneration are present.

The boundary of the tumor tissue is well-defined. Beneath it is inflammatory tissue which contains many young bloodvessels and young connective-tissue cells, and is infiltrated by numerous lymphocytes and leukocytes. So also is the underlying lung tissue. The alveoli are compressed. Few or no air spaces are present in some areas, the lung tissue being solid and compact and infiltrated by pus cells and lymphocytes. In other areas the air sacs are distended and the septa broken through. In none of the sections examined are any tumor cells found in the lung tissue.

A section made from the mushy soft material between the lung and the parietal wall shows this tissue to consist of the same elements as the original tumor.

Mediastinal Lymph Nodes. Sections from two lymph nodes were taken. Both consist chiefly of sarcomatous tissue, which has replaced the lymphoid tissue. Only in a few places near the capsule

a small rim of lymphoid tissue is left. In one node the center is degenerating.

A section taken from the diaphragm includes the soft sarcomatous material between it and the heart. The diaphragm is not invaded with tumor cells.

Liver. The parenchymatous cells are cloudy and indistinct. They contain many fat globules of large size, and large areas of liver tissue are replaced by fat cells. Many pus cells are present, but they are chiefly contained in the sinusoids and vessels.

Spleen. The spleen is diffusely infiltrated with pus cells.

Pancreas. The bloodvessels contain many leukocytes. The parenchymatous tissue is cloudy.

Adrenals. The adrenal cells show degenerative changes. The medulla is richly infiltrated with lymphocytes and moderately with pus cells. The pus cells are numerous and in the bloodvessels. The large numbers of leukocytes found in the bloodvessels in the different organs is explained by the high white count, which three days before death was 122,000.

The microscopic examination proves that we have a sarcoma of the the mixed cell variety. The tumor is entirely pericardial. The myocardium is nowhere involved in the sections examined, which were taken from different places in the heart muscle. Microscopic examination as well as gross inspection shows that the tumor is covered by a membrane consisting of two layers, the visceral and parietal pericardium. The tumor is peripheral to the subepicardial fat, and it is probable that it originated in the subepicardial adipose tissue.

In two sections the pericardium covering the tumor contains sarcoma cells, but on its external surface a thin layer of sarcomatous tissue is present, making this surface irregular.

It is evident that the original tumor is the big tumor on the surface of the heart, and the tumor tissue found in the pericardium, pericardial fat, the pleura and in the mediastinal glands are metastases for the following reasons:

1. On account of the large size of the cardiac tumor and its well-defined structure.
2. It is the oldest of the sarcomatous tissue examined, as shown by the cystic, necrotic areas which are seen on microscopic and macroscopic examination.
3. The cells of the sarcomatous tissue in the pleura and lymph glands are younger in appearance, more active and do not present such marked degenerative changes.

DISCUSSION. It is a rather difficult undertaking to give a review of the literature of sarcoma of the heart, for some of the cases reported are obviously not sarcomas, and with others there is no proof that they are primary. Among the latter I count the case of G. Impacciante¹⁸ and of Williams and Miller.¹⁹ Both are

cases of sarcoma of the mediastinum. In the latter case a tumor was found filling up nearly the entire chest cavity, adhering to the anterior surface of the heart, to the sternum and the diaphragm. In such a large general sarcoma of the mediastinum it is difficult to determine its origin. Other cases which are questionable as to their origin have been reported as primary sarcomas of the heart.

Some writers classify as sarcomas cases which are not reported as such, as the case of Zanders,²⁰ who reported a fibroma of the heart and remarked that in some places the cells were spindle-shaped, the structure approaching that of a spindle-cell sarcoma. Similarly, Crawford²¹ reported a tumor of the heart, believing it to be a blood-clot, but stating that a sarcoma had to be considered.

Byrom Bramwell,²² in 1875, reported a case of sarcoma of the heart, and later in his book on *Diseases of the Heart and Thoracic Aorta* corrected the diagnosis and stated that it was not a primary but a secondary tumor.

A myxosarcoma hematodes was reported by Wiegand.²³ Most writers class this case as myxoma. The same is to be said of Salvioli's²⁴ case. Prudhomme's²⁵ case, counted by Fraenkel as primary sarcoma, seems to have been a secondary melanotic sarcoma to judge from the clinical history and pathological description, but no microscopic examination was made. Of the cases reported in recent years, those of Méroz and Ménétrier appear doubtful to Thorel.²⁶

Reviews of the literature have been made by Bodenheimer, Berenson, Fraenkel, Link, Karrenstein, Ehrenberg and others. In fact, nearly every writer who reports a new case mentions some of the cases which were previously reported. Ehrenberg, who gives the most complete review of sarcoma of the heart, in 1911, reported 19 cases. Two of his cases, those of Byrom Bramwell and Crawford, are not included in the following summary. There are some cases which are not controlable in a clinical or pathological respect, but it is difficult to know where to draw the line. In some the description is incomplete or unclear, in some the clinical description is not obtainable or no microscopic examination has been made. Birch-Hirschfeld's case is only mentioned.

Of the 30 cases which I was able to find in the literature only 3, including that of the author, are reported in American journals. The majority, 19 cases, are found in the German medical literature, 3 are English publications, 4 are reported in French, 1 in Italian and 1 in Swedish. It seems that tumor of the heart furnishes a favorite subject for dissertations for obtaining the M.D. degree. Eight cases among these 31 are reported as dissertations.

A correct clinical diagnosis was not made in any instance. Seven times the diagnosis of tumor of the mediastinum was made, once of intrathoracic tumor and once of cancer of the lung. Myocarditis was the diagnosis 4 times and pericarditis with effusion twice.

Besides these diagnoses a good many others were made which were not related to the heart disease, as encysted effusion and solidification of the lung, bronchopneumonia, edema of the lung, pleurisy with effusion, tuberculosis serosa, hemiplegia, bronchitis, scarlet fever, diphtheria, aneurysm, etc.

Sarcoma of the heart occurs at all ages. The two youngest were three and seven years old respectively; the oldest were seventy-two, seventy-six and seventy-nine years of age. All other patients were between the ages of eighteen and fifty-eight.

As regards the sex this disease apparently favors the male. Of our cases 18 were males and 10 females.

I am not able to give a detailed description and a complete picture of the clinical condition in the appended table on account of lack of space, and only mention those symptoms and signs which seem to me the most important, but it is evident that in the majority of cases the symptoms are produced by seriously disturbed cardiac activity. In most cases we find some of the following symptoms, venous congestion and stasis, cyanosis, pleural or pericardial effusion, edema of the legs and other parts of the body, edema of the lung, ascites, dyspnea, palpitation of the heart, irregular pulse, cough, etc. In only a few cases were heart murmurs heard. Repeated aspirations of bloody fluid from the pleural cavity were done only in Raw's and the author's cases. Repeated aspirations of bloody fluid from the pericardial cavity, which, according to Fraenkel, is of considerable diagnostic importance, was done only in his own case. Sudden death without previous symptoms occurred in 3 cases. In 21 cases the disease lasted from one month to three and a half years.

From a histological point of view there are:

Spindle-cell sarcomas	10
Round-cell sarcomas	6
Giant-cell sarcomas	4
Myxosarcomas	3
Fibrosarcomas	3
Mixed-cell sarcomas	2
Angiosarcoma	1
Lymphosarcoma	1

Eight cases of our series, including that of the author, are sarcomas of the pericardium. Of these Broadbent's case is apparently confined to the pericardium (only the chest was examined). In Drysdale's case and Lambert's case there was a general sarcomatous infiltration of the myocardium.

The cystic tumor reported by Kaak was in the upper part of the pericardium, connected with the pericardium and the large veins. Redtenbacher's angiosarcoma of the pericardium contained a cavity which was in communication with the right ventricle. In Schöppler's case there was a general sarcomatosis of the epicardium, the entire heart being enveloped in sarcomatous tissue. In Tobie-son's case the tumor masses were mostly on the surface of the

pericardium; these tumors were chiefly in the pericardial cavity or on the surface of the pericardium. The author's case seems to take a special place by taking its origin in the subepicardial areolar tissue, being covered by both layers of the pericardium.

The seat of the tumor was as follows:

	Cases.
Pericardium	8
Right auricle	11
Left auricle	6
Right ventricle	1
Right and left auricle	1
Ventricular septum	1
Aortic valve	1
Left ventricle and auricle	1

The size varied from that of a walnut to that of a child's head.

Metastases were found in 10 cases as follows:

	Cases.
In the liver	2
In the pancreas	2
In the lung	1
In the suprarenals	2
In the pleura and mediastinal lymph nodes	1
In the tracheal lymph nodes and suprarenals	1
In the lung and pararenal tissue	1

Among the postmortem findings, stasis due to interference with the circulation was the most common condition. Pleural effusion was found in 13 autopsies (four times bloody); pericardial effusion in 10 cases (five times bloody). The pericardium was partly or entirely obliterated 5 times.

SUMMARY OF REPORTED CASES.

No. 1. Baldwin, *Jour. Am. Med. Assn.*, 1910, lx, 635. Clinical diagnosis: Encysted effusion or solidification of bases of both lungs. Age and sex: thirty-four years; male. Main clinical symptoms: Dyspnea; edema of ankles; diffuse rales in both sides; flatness of both bases; bloody expectoration; cough; enlargement of heart. Duration and nature of tumor: Five months; large spindle-cell sarcoma. Location and size: Left auricle; 5 x 6 x 7 cm. Other postmortem findings: Organized blood-clot at base of left lung; dilatation of right side of heart. Remarks: A pedunculated tumor originating from the margin of the pulmonary veins. No metastases.

No. 2. Binder, *Frankfurter Ztschr. f. Path.*, 1914, xv, 194. Clinical diagnosis: Aneurysm; tumor of mediastinum. Age and sex: Thirty-three years; male. Main clinical symptoms: Dyspnea; edema of face, thorax, later of legs; venous telangiectasis of abdomen and thorax; no ascites. Duration and nature of tumor: Fifty days; spindle-cell sarcoma. Location and size: Right auricle; right auricle nearly filled. Other postmortem findings: Bilateral pleural serous effusion. Remarks: A tumor which is

pedunculated, of the size of a walnut, hangs down from the right auricle into the vena cava. No metastases.

No. 3. Birch-Hirschfeld, *Lehrbuch der Path.*, 1876, p. 360. Nature of tumor: Giant-cell sarcoma. Location and size: Right auricle; walnut. Remarks: Origin in endocardium and right auricle. No other data.

No. 4. Bodenheimer, *Dissertation*, Bern, 1865. Clinical diagnosis: Heart disease of unknown origin. Age and sex: Forty-four years; male. Main clinical symptoms: Edema of upper and lower extremities; ascites; pericarditis with effusion; dulness of both bases; rales; sanguino-muco-purulent expectoration; sudden death. Duration and nature of tumor: Two months; sarcoma. Location and size: Right auricle mainly; 30 x 20 cm. Other post-mortem findings: Pericarditis with effusion; right pleural effusion. Remarks: A tumor consisting of about 20 nodules on the anterior surface of the right and left auricle, growing into the cavity of the right auricle. No metastases.

No. 5. Broadbent, *Tr. Path. Soc.*, London, 1889, lxxxii, 39. Age and sex: Twenty-three years; male. Main clinical symptoms: Shortness of breath; signs of fluid in left chest and pericardium. Duration and nature of tumor: Three months; lymphosarcoma. Location: Pericardium. Other postmortem findings: Bloody pericardial effusion; fibrous pleurisy. Remarks: Pericardium 0.5 to 1.5 cm. thick; does not collapse after fluid is removed. No other part examined, but there did not seem to be any metastases.

No. 6. Crescenzi, *Monatschr. f. Kinderheilk.*, 1906-07, v, 369. Clinical diagnosis: Scarlet; diphtheria; bronchopneumonia. Age: Three years. Main clinical symptoms: Fever; scarlet eruption; diphtheria bacillus and streptococcus culture from throat; pharyngitis; bronchopneumonia. Duration and nature of tumor: Three months; sarcoma globocellulare. Location: Ventricular septum. Remarks: An intramural growth; does not reach endocardium. Tumor is in initial period of development. Posterior ventricular walls slightly infiltrated. No metastases.

No. 7. Drysdale, *Tr. Path. Soc.*, London, 1903, liv, 311. Age and sex: Forty-three years; female. Main clinical symptoms: Dyspnea; edema of legs; in state of collapse on admission; puerperal insanity; died after three days. Duration and nature of tumor: Eight months; round and oval-cell sarcoma. Location: Pericardium infiltrating myocardium extensively. Other postmortem findings: Obliterative pericarditis; pulmonary artery compressed. Remarks: Metastases in liver.

No. 8. Escher, *Dissertation*, Leipzig, 1909. Clinical diagnosis: Emphysema of lung; dilatation of heart. Age and sex: Seventy-two years; female. Main clinical symptoms: Shortness of breath; edema of legs; later edema of left arm and left chest. Duration and nature of tumor: One year; round-cell sarcoma. Location: Right auricle mainly. Other postmortem findings: Edema of legs;

arteriosclerosis; subpleural hemorrhage. Remarks: Pericardium obliterated and infiltrated with tumor tissue; tumor nodules on surface of pericardium. Metastases in tracheal lymph nodes and in suprarenal.

No. 9. Ehrenberg, *Deutsch. Arch. f. klin. Med.*, 1911, ciii, 293. Clinical diagnosis: Tumor of mediastinum, with compression of superior vena cava. Age and sex: Forty-nine years; male. Main clinical symptoms: Dyspnea; cyanosis; edema of upper half of body, head and upper extremities; enlargement of veins on upper abdomen and thorax; roentgen-ray; shadow to right of sternum. Duration and nature of tumor: Four months; polypoid giant-cell sarcoma. Location and size: Right auricle; right auricle filled. Other postmortem findings: Right pleural serous effusion; serous pericardial effusion. Remarks: Venæ cavæ, part of anomya and azygos dextra filled by tumor tissue.

No. 10. Ely, *Thèse de Paris*, 1877, cited from Ehrenberg⁴ and Méroz.¹¹ Age and sex: Twenty-eight years; male. Main clinical symptoms: Had been in hospital several times for bronchitis; died suddenly without sickness preceding death. Duration and nature of tumor: Sudden death; sarcoma. Location: Anterior wall of left ventricle. Remarks: No metastases.

No. 11. Erickson, *Upsala Läkarf. Förh.*, 1908, Band xiii, Hef; 6, cited from Méroz.¹¹ Clinical diagnosis: Myocarditis; bronchitis; pulmonary edema. Age and sex: Thirty-six years; male. Main clinical symptoms: Symptoms of myocarditis, bronchitis and pulmonary edema. Nature of tumor: Fibrosarcoma. Location: Left auricle. Remarks: A fibroma, with sarcomatous changes marked in places. No metastases.

No. 12. Fuhrman, *Dissertation*, Marburg, 1899. Age and sex: Seven years; female. Main clinical symptoms: Sudden death; had had a slight headache for two days. No other symptoms. Duration and nature of tumor: Sudden death; spindle-cell myxosarcoma. Location: Aortic valve. Remarks: Grape-like appearing tumors, obliteration of the right coronary artery by a tumor in front of it. Left coronary artery is occluded by a plug of tumor tissue. No metastases.

No. 13. Fuhrman (second case), *Dissertation*, Marburg, 1899. Age and sex: Thirty-four years; male. Main clinical symptoms: Palpitation of heart; cough; fatigue; weakness; frothy sputum; cyanosis; dyspnea; no edema; no murmurs. Duration and nature of tumor: Six months; spindle-cell sarcoma with giant cells. Location: Left auricle. Other postmortem findings: Left pulmonary vein obliterated by tumor. Remarks: This case had been reported as a myoma by Justi. Two tumors in the left auricle arising from the median and lateral wall. Small tumor the size of a bean on the mitral valve. No metastases.

No. 14. Fraenkel, *Festschr. zur Eröffnung d. Krankenhauses Hamburg-Eppendorf*, 1889, p. 102. Clinical diagnosis: Pericardi-

tis, left serous; infarct in right lower lobe of lung. Age and sex: Eighteen years; female. Main clinical symptoms: Pericarditis with bloody effusion; pleurisy with serous effusion; dyspnea; cyanosis; weak irregular pulse; bloody sputum; flatness in both lower lobes. Duration and nature of tumor: Fifty days; spindle-cell sarcoma. Location and size: Right auricle; 8 x 7 x 4.5 cm. Other postmortem findings: Atelectasis of left lower lung. 1.5 liters of serous fluid in the pericardium. Remarks: The pericardium was aspirated four times; 300, 1000, 80 and 750 c.c. of bloody fluid were obtained. No metastases.

No. 15. Fraenkel, *München. med. Wchnschr.*, 1901, No. 1, xlviii, 648 (summary). Main clinical symptoms: Symptoms of seriously disturbed cardiac activity. Nature of tumor: Mixed giant-cell sarcoma. Location: Apex of right ventricle. Remarks: No metastases.

No. 16. Geipel, *Zentralbl. f. allg. Path.*, 1899, x, 846. Age and sex: Fifty-three years; female. Main clinical symptoms: Left-sided apoplexy. Nature of tumor: Round-cell sarcoma. Location and size: Right auricle; 5.5 x 4.5 x 4 cm. Other postmortem findings: Pericardial cavity obliterated except for an area the size of the palm of the hand; destruction of last half of corpus striatum, the largest part of the internal capsule and insula. Remarks: Right auricle nearly filled by tumor, which is attached by a pedicle to the interauricular septum and adjacent area; right ventricle wall also infiltrated. No metastases.

No. 17. Horneffer and Gautier, *Revue méd. de la Suisse romande*, 1913, xxxiii, 57. Clinical diagnosis: Bronchitis; cardiorenal disease; myocarditis. Age and sex: Forty-three years; male. Main clinical symptoms: Symptoms of bronchitis for two years; bloody sputum; dizziness; weak limbs; vertigo; fainting spells; arrhythmia; murmurs at base of heart; dyspnea. Duration and nature of tumor: Two years intermittently; myxosarcoma. Location and size: Left auricle; 6 x 5 x 2 cm. Other postmortem findings: Pericardial effusion; right pleural effusion. Remarks: Cauliflower-like pedunculated growth reaching down to mitral valve and sending prolongations through it. The tumor grows through the auricle wall appearing on its surface. No metastases.

No. 18. Hottenroth, *Dissertation*, Leipzig, 1870. Clinical diagnosis: Chronic bronchitis; pleural effusion. Age and sex: Seventy-nine years; female. Main clinical symptoms: Marantic and emaciated; various kinds of rales; signs of fluid in chest. Nature of tumor: Giant-cell sarcoma. Location and size: Right auricle; hen's egg. Other postmortem findings: Right auricle dilated; vena cava dilated. Remarks: Growth is cauliflower-like. No metastases.

No. 19. Juergens, *Berl. klin. Wchnschr.*, 1891, xxviii, 1031. Age and sex: Thirty-six years; male. Duration and nature of tumor: Sudden death on street; fibrosarcoma. Location: Right auricle

mainly. Other postmortem findings: Tricuspid valve narrowed. Remarks: Diffuse infiltration of wall of right auricle, tendons of tricuspid valve and wall of right ventricle.

No. 20. Kaak, *Dissertation*, Kiel, 1904. Clinical diagnosis: Myocarditis with marked disturbance in compensation. Age and sex: Twenty-seven years; male. Main clinical symptoms: Cough and pain in both axillæ; dyspnea; edema of legs, back and eyelids; ascites; dulness at bases of both lungs; pleuritic friction rub. Duration and nature of tumor: Four weeks; myxocystosarcoma. Location: Pericardium. Other postmortem findings: Two hemorrhagic infarcts in lung; edema of bases of lungs; bilateral pleural effusion; ascites; edema. Remarks: The tumor is in the upper part of the pericardial cavity connected with the pericardium and large vessels. It is partly cystic; one large cyst, 11 cm. long, hangs down from the lower portion of the tumor. Two thoracenteses done, 1700 c.c. of yellowish fluid at second aspiration.

No. 21. Lambert, *New York Med. Jour.*, 1898, lxxvii, 210. Clinical diagnosis: Pneumonia; pericardial effusion; bilateral pleurisy, with effusion; mediastinal tumor at root of right lung. Age and sex: Thirty-nine years; male. Main clinical symptoms: Signs of pneumonia, which only partly cleared up; developed bilateral serous effusion; cyanosis; ascites; pericardial effusion; edema of upper part of body. Duration and nature of tumor: Thirty-seven days; small round-cell sarcoma. Location: Visceral surface of pericardium; myocardium diffusely infiltrated. Other postmortem findings: Fibrinous pericarditis, with bloody effusion. Remarks: Nodular growth covers inner surface of pericardium; wall of left ventricle extensively infiltrated; nodules in other parts of myocardium. Metastatic nodule in head of pancreas.

No. 22. Link, *Ztschr. f. klin. Med.*, 1909, lxxii, 272. Clinical diagnosis: Tumor of mediastinum. Age and sex: Twenty-three years; male. Main clinical symptoms: During the twenty months preceding death he was four times in the hospital with dyspnea, pain in the heart region, cough, cyanosis, pericarditis, pleural effusion; last time had edema, thrombosis of external jugular vein bloody sputum. Duration and nature of tumor: Twenty-one months; spindle-cell sarcoma. Location and size: Right and left auricle; heart and tumor were size of a child's head. Other postmortem findings: Pericardial cavity mostly obliterated; bilateral pleural effusion. Remarks: Upper border of the tumor, which is at innominate vein, measures 15 cm. Almost nothing is left of the walls of the auricle. The walls of the ventricle are preserved. Roentgen-ray showed increase in shadow of heart to right and left in upper part.

No. 23. Ménétrier, *Acad. de méd. de Paris*, March 7, 1911 (cited from *Zentralbl. f. Herzkrank.*, iii, 208.) Age and sex: Thirty-five years; male. Main clinical symptoms: Edema of body below diaphragm; dyspnea; bloody pleural effusion; hemoptysis. Nature

of tumor: Myxosarcoma, with fusiform cells. Location and size: Left auricle; 6 cm. Other postmortem findings: Infarcts in lung; hemorrhagic effusion in pleural cavity. Remarks: Tumor compresses right auricle and interferes with circulation. Edema entirely below diaphragm suggests compression of inferior vena cava.

No. 24. Méroz, *Thèse*, Geneva, 1911. Clinical diagnosis: Mitral regurgitation; left pleurisy; cancer of lungs. Age and sex: Fifty-five years; female. Main clinical symptoms: Pain in left side; pain on respiration; dyspnea; scattered rales and dullness; mitral regurgitation; systolic murmur; pleural effusion; edema of lungs. Duration and nature of tumor: Two months; spindle-cell sarcoma. Location and size: Left auricle; hen's egg. Other postmortem findings: Left pleural cavity contains 2000 c.c., and pericardium 100 c.c. of purulent fluid. Remarks: The tumor hangs down into the left ventricle through the enlarged mitral valve. No metastases.

No. 25. Raw, *British Med. Jour.*, 1898, ii, 1335. Clinical diagnosis: Tumor of mediastinum. Age and sex: Forty-three years; female. Main clinical symptoms: Continual pain in chest for three and one-half years; dyspnea; ascites; edema of legs; dullness in right chest; outward displacement of heart; hemothorax; murmur at base of heart. Duration and nature of tumor: Three and a half years; fibrosarcoma. Location and size: Right auricle 3 x 3 x 3¼ cm. Other postmortem findings: Bacillus *aërogenes capsulatus* in blood; lumbar veins enlarged; inferior vena cava nearly empty. Remarks: Repeated aspirations of thorax gave bloody fluid from chest. Growth extends continuously from right auricle through inferior vena cava to under surface of liver. Microscopically it appears as fibroma, containing clusters of round cells; this and metastasis in liver suggests fibrosarcoma.

No. 26. Redtenbacher, *Wien. klin. Wchnschr.*, 1889, ii, 214. Clinical diagnosis: Serous membrane tuberculosis. Age and sex: Twenty-two years; male. Main clinical symptoms: Symptoms of pericarditis; frothy expectoration; effusion into both pleural sacs; later into abdomen; dyspnea and hydrops very marked. Duration and nature of tumor: Four months; angiosarcoma of pericardium. Location and size: Pericardium; palm of hand. Other postmortem findings: The abdomen contains 6 liters, the right pleural cavity ½ liter, the left 2 liters of serous fluid; the heart 100 c.c. of bloody fluid; the pericardium is adherent to the heart except at the apex. Remarks: Over right auricle and part of right ventricle is a blood-containing cavity communicating with right ventricle. Metastases in right lung.

No. 27. Schoeppler, *München. med. Wchnschr.*, 1906, xlv, 2197. Clinical diagnosis: Hemiplegia. Age and sex: Seventy-six years; female. Main clinical symptoms: Unconscious on admission; demented and delirious; pericardial friction rub; systolic murmur at apex; right-sided paralysis, which disappeared. Nature of

tumor: Round-cell sarcoma of epicardium. Location: Covers entire heart. Other postmortem findings: Fibrinous pericarditis. Remarks: Died three months, twenty-four days after admission; no history obtainable; the entire heart is enveloped in nodular irregular sarcomatous tissue. Metastasis on left surface of suprarenal.

No. 28. Sternberg, *Zentralbl. f. Herzkrank.*, 1910, ii, 151. Clinical diagnosis: Myocarditis. Age and sex: fifty-eight years; female. Main clinical symptoms: Dyspnea; edema of ankles; enlargement of heart; incomplete examination on account of low condition of patient. Duration and nature of tumor: Two months; spindle-cell sarcoma. Location: Wall of left ventricle; in right and left auricles. Other postmortem findings: Hemorrhagic fluid in right pleural cavity; infarct in lung; hemorrhagic pericardial effusion; Thrombosis of many branches of pulmonary artery. Remarks: Vena magna cordis filled with tumor tissue which projects like a polypoid growth into right auricle. A large tumor nodule in left auricle grows out of right pulmonary vein, which is completely filled with tumor tissue. Metastasis in tail of pancreas.

No. 29. Tobieson, *Ztschr. f. klin. Med.*, 1912, lxxv, 53. Clinical diagnosis: Intrathoracic tumor. Age and sex: Eighteen years; male. Main clinical symptoms: Irregular heart; fever; friction rub over nipple; cough; decreased breathing beneath scapula; enlargement of heart; systolic murmur at pulmonary region; thrombosis of jugular vein; edema; cyanosis; dyspnea; pleural effusion; gangrene of nose. Duration and nature of tumor: Nine months; spindle-cell predominating. Location and size: Internal surface of pericardium; man's head. Other postmortem findings: Bilateral pleural effusion (bloody); pericardium filled with coagulated blood. Remarks: The tumor masses mostly on the internal surface of the pericardium are flat or nodular; the vena cava superior is completely compressed and no lumen is left. Metastases in lung.

No. 30. Weiss, *Gazz. med. ital. Prov. Venete*, 1880, xxiii, 301. Clinical diagnosis: Tumor of anterior mediastinum; compression of pulmonary artery and descending vena cava. Age and sex: Thirty-eight years; male. Main clinical symptoms: Cyanosis; edema of upper part of body, head and upper extremities, especially the left side; decreased pericardial dullness; dullness at bases of lungs; cardiac palpitation; dyspnea; left pleural effusion. Duration and nature of tumor: Thirty-four days; large round cell predominating. Location and size: Right auricle mainly; child's head. Other postmortem findings: Edema of upper part of body, lung and cerebrum; thrombus of descending vena cava; interstitial hepatitis; obliterated pericardium; bilateral serous pleural effusion. Remarks: The tumor with the heart and the obliterated pericardium formed a large mass the size of a child's head. The tumor was mainly in the right auricle and had broken through the interauricular septum; myocardium of right auricle largely replaced by

tumor tissue, that of the other chambers extensively infiltrated. Tumor masses enveloped the heart. Metastases in lung and pararenal tissue.

No. 31. Perlstein. Clinical diagnosis: Tumor of mediastinum. Age and sex: Forty-three years; male. Main clinical symptoms: Dyspnea; cough; perspiration; restlessness; thirst; weakness; hemothorax. Duration and nature of tumor: Thirty-one days; Mixed-cell sarcoma. Location and size: Pericardium; 13 x 8 x 5 cm. Other postmortem findings: Chronic obliterative pericarditis; hemothorax; anemia; interstitial pneumonia; lobar pneumonia; chronic emphysema. Remarks: A well-defined tumor originating in the subepicardial adipose tissue located essentially between heart and epicardium, invading the pericardial membranes and fat. The myocardium is not invaded. Metastases in mediastinal lymph nodes and in pleura.

CONCLUSIONS. 1. Only 30 cases of sarcoma of the heart were found after a careful search of the literature. To these is added a case in which the tumor originated apparently in the subepicardial areola tissue.

2. There is no characteristic clinical picture for the condition. The symptoms are mostly those of seriously disturbed cardiac activity. Excessive and repeated hemothorax was the most striking clinical feature of the case reported.

3. Sarcomas of the heart occur at all ages, but are most common in the vigorous years of life.

4. Histologically all types of sarcoma have been reported. The spindle-cell variety is the one most often found.

5. They occur more often in the auricles than in the ventricles, and more frequently on the right than on the left side.

6. Among the postmortem findings, pericardial and pleural effusions and edema are common.

BIBLIOGRAPHY.

1. Tedeschi: Prager med. Wehnschr., 1893, xviii, 121.
2. Berthenson: Arch. f. path. Anat., 1893, cxxii, 390.
3. Link: Ztschr. f. klin. Med., 1908-1909, lxxvii, 272.
4. Ehrenberg: Deutsch. Arch. f. klin. Med., 1911, ciii, 293.
5. Bryant: Johns Hopkins Hosp. Bull., 1907, xviii, 474.
6. Karrenstein: Virchows Arch., 1908, civ, 127.
7. Schöppler: München. med. Wehnschr., 1906, liii, 2197.
8. Dietrich: Arbeiten aus d. Gebiete der Bact. u. Path. aus d. path. Anat., Inst., v. Tübingen, 1914, ix, 87-93.
9. Foerster and Garnieri: Arch. p. le sc. med., No. 6, vol. x.
10. Joel: Virchows Arch., 1890, cxxii, 381.
11. Méroz: Diss. Genève, 1911.
12. Adami: Principles of Pathology, 1909, p. 158.
13. Bodenheimer: Diss. Bern., 1865.
14. Osler: Modern Medicine, Diseases of the Heart, iv, 130.
15. Nothnagel: Encyclopedia of Diseases of the Heart, 1909, p. 667.
16. Fraenkel: Festschrift z. Eröffnung des Krankenhauses Hamburg-Eppendorf 1889, p. 102.
17. Eichhorst: Specielle Path. u. Therapie, 1904, 5te Abt., Bd. i.
18. Impacciante: Lo Sperimentale, 1882, lxi, 3-11.

19. Williams and Miller: *New York Med. Jour.*, 1900, lxxi, 537.
20. Zanders: *Virchows Arch.*, 1880, lxxx, 507.
21. Crawford: *London Pathological Society*, 1898, xlix, 37.
22. Byrom Bramwell: *British Med. Jour.*, 1875, ii, 665.
23. Wiegand: *St. Petersburg Med. Wehnschr.*, 1876, No. 19, i, 3.
24. Salvioli: *Rivista Clin. d. Bologna*, 1878, No. 10.
25. Prudhomme: *Gaz. des Hôp.*, 1867, xl, 30.
26. Thorel: *Ergebnisse der Allg. Path. und pathologischen Anatomie d. M. u. T.*, 1915, xvii², 685.
27. *Virchows Archiv*, 1856, i, 215.

STUDIES IN CHOLELITHIASIS.

I. THE DISTURBANCES OF THE CHOLESTERIN METABOLISM AS A FACTOR IN GALL-STONE FORMATION.

BY MARCUS A. ROTHSCHILD, M.D.,

NEW YORK,

AND

ABRAHAM O. WILENSKY, M.D.,

NEW YORK.

(From the Pathological Laboratory of Mount Sinai Hospital.)

In this communication our present knowledge of the cholesterin metabolism is summarized and the importance of a hypercholesterinemic state both in the blood and bile as an etiological factor in the production of gall-stones is emphasized. The various elements in gall-stone formation are studied. These are the relationships of food to the cholesterin content of the blood and bile and the effect of bacterial infection and of an unknown variable factor which in a later communication will be discussed under the term of "cholesterin diathesis."

BILE. The chemical composition of bile has been investigated by numerous workers and the relative proportions of its various constituents have been found to be variable. This is readily explained when one analyzes the chemical methods in use during earlier periods as well as the various factors present in the individual cases at the time the analyses were made. Necessarily for this purpose biliary fistulæ of one kind or another must be made, and these immediately introduce abnormal factors. In addition, in practically all of the cases studied, pathological conditions have existed. Frerichs¹ examined the bile of two healthy people who had been killed accidentally; von Gorup-Besanez² examined the bile of a man, aged forty-nine years, and of a woman, aged twenty-nine years. Hammersten³ examined the human liver bile in 3 cases.

¹ Hoppe-Seyler: *Physiologische Chemie*, p. 299.

² *Ibid.*

³ *Physiological Chemistry*, English translation, New York, 1906.

The results of all of these are tabulated, the figures indicating parts per thousand:

TABLE I.—FRERICHS.⁴

	1.	2.
Water	860.0	859.2
Solids	140.0	140.8
Bile salts	72.2	91.4
Mucus and pigments	26.6	29.8
Cholesterin	1.6	2.6
Fat	3.2	9.2
Inorganic substances	6.5	7.7

TABLE II.—VON GORUP-BESANEZ.⁵

	1.	2.
Water	822.7	898.1
Solids	177.3	101.9
Bile salts	107.9	56.9
Mucus and pigments	22.1	14.5
Cholesterin and fat	47.3	30.9
Inorganic substances	10.8	6.2

TABLE III.—HAMMARSTEN.⁶

	1.	2.	3.
Solids	25.200	35.260	25.400
Water	974.800	964.740	974.600
Mucin and Pigments	5.290	4.290	5.150
Bile salts	9.310	18.240	9.040
Taurocholate	3.034	2.079	2.180
Glycocholate	6.276	16.161	6.860
Fatty acids from soaps	1.230	1.360	1.010
Cholesterin	0.630	1.600	1.500
Lecithin and fat	0.220	1.530	1.260
Soluble salts	8.070	6.760	7.250
Insoluble substances	0.250	0.490	0.210

Our investigations have been devoted to determinations of the cholesterin content of bile obtained from biliary fistulae leading into the gall-bladder, the hepatic or the common bile ducts, made during the course of operations upon patients for various diseased conditions of the bile passages with and without stone formation. The methods of Autenrieth and Funk⁷ and Bloor⁸ were employed for these analyses, and occasionally these were verified by recourse to the Windaus⁹ method. The older methods are subject to much criticism. Our determinations were made in duplicate and were checked up in various ways. Many determinations were made in each case, and the comparative results may therefore be regarded as true indices. Our results in normal bile have given values for the cholesterin contents varying between 20 and 80 mg. per 100 c.c.

⁴ Loc. cit.⁵ Loc. cit.⁶ Loc. cit.⁷ München. med. Wchnschr., 1913, lx, 1243.⁸ Jour. Biol. Chem., 1915-16, xxiv, 227.⁹ Ztschr. f. physiol. Chem., 1910, lxxv, 110.

It is proper to consider the bile as a colloidal solution, the cholesterin being held in suspension by means of the bile salts, acids, fats and lecithin dissolved in the same. Such a compound mixture is subject to the ordinary physical and chemical laws. Precipitations of any of the ingredients may follow supersaturation or a disturbance of the normal equilibrium. It is conceivable that a bacterial infection causing an inflammatory response in the gall-bladder wall, with its consequent exudation of electropositive serum-albumin, will also cause the precipitation of the ingredients of an electro-negative solution.

The supersaturation may be only relative, owing to the fact that the amount of bile salts in solution may be above or below the normal content. In test-tube experiments it has been shown that an increase of the dissolved bile salts may enable the bile to take up an extraordinary amount of cholesterin. The converse of this has also been shown.

The idea of supersaturation was well illustrated in the case of a patient in whom at operation the gall-bladder was drained. The bile obtained from the gall-bladder and that which drained away in the first twenty-four hours was, macroscopically, a thick emulsion which, microscopically, was seen to be due to large masses of cholesterin crystals. The remarkable figure of 850 mg. of cholesterin for each 100 c.c. of bile was obtained.

The same idea has also been corroborated in some animal experiments. Anitschkow and Chalатов¹⁰ have shown that when the cholesterin content of the bile of rabbits becomes markedly increased, concretions are deposited within the gall-bladder consisting of pure cholesterin. Dewey¹¹ has also recently produced small stones in the gall-bladders of hypercholesterinized animals.

It has usually been found that the bile obtained from the gall-bladder has a higher cholesterin content than bile obtained from the ducts. This, however, is only true for the first two or three days after drainage is instituted. The discrepancy is accounted for by the fact that a certain amount of stagnation takes place in the gall-bladder as well as by an increase in the cholesterin of the inflammatory exudate.

BLOOD. In ascertaining the cholesterin content of the blood, similar methods were employed, and in normal persons the values were found to vary between 150 and 180 mg. per 100 c.c. of blood. Our results have corresponded with those of other workers, as follows: Chauffard, Laroche and Grigaut,¹² 150 to 180 mg. per 100 c.c. blood; Widal, Weill and Laudat,¹³ 174 to 195 mg. per 100 c.c. blood; Bacmeister and Havers,¹⁴ 110 to 180 mg. per 100 c.c. blood.

¹⁰ *Centralbl. f. allg. Path.*, 1913, xxiv, 1.

¹¹ *Arch. Int. Med.*, 1916, xvii, 757.

¹² *Compt. rend. Soc. de biol., Paris*, 1911, lxx, 336.

¹³ *Soc. Biol.*, 1911, lxiv, 883.

¹⁴ *Deutsch. med. Wchnschr.*, 1914, No. 8.

THE RELATIONSHIP OF FOOD, BLOOD AND BILE. The question as to whether the cholesterin of the food is absorbed is of paramount importance. The investigations of Doree, Ellis, Fraser and Gardner¹⁵ offer excellent proof of such absorption. Divergent results have been obtained by other authors on account of the types of animals employed and because of the artificial conditions produced in the experiments. Pribram,¹⁶ Fraser and Gardner,¹⁷ Grigaut and L'Huillier,¹⁸ Anitschkow and Chalатов,¹⁹ Wasker,²⁰ Weltman and Biach²¹ and Rothschild²² have proved conclusively that cholesterin fed to rabbits is absorbed and that an extensive feeding is followed by an increase in the cholesterin content of the blood. The last named proved further that the cholesterin content of the blood of rabbits must increase to a certain stage before any increase appears in the bile. This was demonstrated in the following table:

TABLE IV—ROTHSCHILD.²³

No.	Cholesterin content of blood in mgm. per 100 c.c.							Cholesterin content of the bile mgm. per 100 c.c.
	Before feeding.	7th day.	14th day.	28th day.	40th day.	59th day.	150th day.	
180	40	90	10-15
183	50	..	98	10-15
170	48	130	35
157	45	280	90
190 A	300	...	
174 A	100	...	
87 A	364	164

It was also shown (Rothschild) that in hypercholesterinemic rabbits, in which unilateral or bilateral adrenalectomy had been performed, the cholesterin content of the bile increased similarly to that of the blood. The same phenomenon was demonstrated in animals starved for varying lengths of time.

Kusumato²⁴ showed that in dogs the cholesterin content of the bile rose after poisoning with toluylendiamin.

In dogs it is more difficult to produce hypercholesterinemic states, inasmuch as the absorbed cholesterin is excreted very rapidly. Furthermore, all experiments in dogs in whom biliary fistulae have been established are practically valueless. Rothschild showed in dogs that with occlusion of the common bile duct, cholesterin in the food was poorly absorbed, but that it was more easily absorbed when mixed with bile. In an animal with a biliary fistula the loss

¹⁵ Proc. Roy. Soc., 1908, 1909, 1910, 1912.

¹⁶ Biochem. Ztschr., 1908, vii, 152.

¹⁸ Soc. Biol., lxxiii, 304.

²⁰ Ztschr. f. physiol. Chemie, 1912, 80.

²¹ Ztschr. f. exper. Path. u. Therap., 1913, xiv, 367.

²² Ziegler's Beitrage, 1914-15, 60, 39 and 66.

²⁴ Biochem. Ztschr., 1908, xiii, 334.

¹⁷ Ibid.

¹⁹ Ibid.

²³ Loc. cit.

of cholesterin through the escaping bile as well as the poor absorption brought about by the more or less total exclusion of bile from the intestinal tract brings about a negative balance in which the intake is less than the output.

Important evidence is also available from comparative physiological sources to show the close relationship between the cholesterin contents of food, blood and bile. Herbivora, such as rabbits and guinea-pigs whose food is poor in cholesterin, have a lower cholesterin content in their blood and bile. The quantities are so small that Weltman and Biach²⁵ have even denied its presence in the bile. Dogs and cats, as types of carnivora, whose diets are richer in cholesterin, show a much higher cholesterin content of blood and bile. Pigs, as examples of omnivora, show high cholesterin contents of blood and bile. The conclusions of Weltman and Biach²⁶ in regard to a difference in principle of the cholesterin metabolism of herbivora and carnivora were shown to be unwarranted (Rothschild),²⁷ inasmuch as the difference is only one of degree of activity of the liver as a filter.

In humans, who are omnivorous animals, the cholesterin content of the blood and bile is comparatively high. The actual content varies markedly with different races and the differences are found to correspond closely with the diets of the people. De Langen²⁸ recently reported a series of observations made among the natives of Java, China, Japan and India. The cholesterin content of the bloods of these people was found to average 40 to 50 per cent. less than that of Europeans. This corresponds with the diet, poor in cholesterin, which is customary in those parts of the world. These races, in fact, can be classed with the herbivorous animals in contradistinction to the Europeans, who have omnivorous dietary habits.

In the cases which we have studied it has been usually found that immediately following the making of a complete biliary fistula the cholesterin content of the escaping bile is high. Thereafter it falls irregularly and continuously during the first few days, during which period the diet of the patients consists of fluids devoid of, or poor, in lipid materials. The cholesterin content of the bile begins to rise as soon as fats are added to the diet. So characteristic is this phenomenon that the person making the daily determinations of the cholesterin content of the bile can easily tell on which day the diet of the patients has been increased in fats.

Among the patients who undergo operation for the cure of cholelithic conditions it is found that a certain number develop recurrent symptoms a shorter or longer time after recovery from the operation. In some of these, determinations of the lipid content of the blood has demonstrated a continuously hypercholesterinemic condition. It has been found a matter of ease to cause a large decrease in this

²⁵ Loc. cit.

²⁶ Loc. cit.

²⁷ Loc. cit.

²⁸ Presse médicale, 1916, No. 42, 332.

cholesterin content by simply excluding from the diet all lipoid bodies. Conversely, the cholesterin blood content has always been seen to rise again to high figures whenever these patients have returned to their ordinary diets or whenever, for one or another purpose, the lipoid content of the food administered to these patients has been increased.²⁹

Bacteriology of Gall-stones. Evidence of a bacteriological nature in regard to the causative factor in the mechanism of gall-stone formation has been reported since 1886, when Gallipe³⁰ first suggested the microbic origin of biliary calculi. Eight years previously Bernheim³¹ had drawn attention to the clinical connection between typhoid fever and infection of the biliary passages. Welch,³² in 1890, found colon bacilli and staphylococci in the interior of gall-stones, and three years later Chiari³³ was able to demonstrate the presence of typhoid bacilli. One year later Gilbert and Dominici³⁴ found colon bacilli in 23 out of 70 cases, and later showed experimentally that colon and typhoid bacilli could cause inflammation of the gall-bladder leading to stone formation. Mignot³⁵ succeeded in producing gall-stones in animals by the employment of typhoid, colon and subtilis bacilli and staphylococci and streptococci. Milian and Hanot,³⁶ in 1896, found typhoid bacilli in the center of recently formed stones. Cushing, Halstead, Richardson and others have contributed useful facts in the connection between typhoid fever and gall-stone formation.³⁷

The recent work of Rosenow³⁸ in the bacteriology of gall-stones and in the production of experimental cholecystitis by the injection of streptococci is of much interest. It is necessary to remember that these two conditions, while frequently coexisting, are not necessarily a part of the same pathological process, inasmuch as they can and do occur independently of one another. In the examination of a large number of stones it is of special interest to point out that Rosenow obtained sterile cultures from four typical cholesterin stones, while in the mixed stones he obtained a variety of organisms. This lends rather strong support to the theory of the non-bacterial origin of pure cholesterin stones.

The discussion of the last factor indicated in the opening paragraph of this communication is reserved for a future paper. Suffice

²⁹ These postoperative studies will be reported in a later communication.

³⁰ Compt. rend. Soc. de biol., Paris, 1886, p. 116.

³¹ Dict. Encyclop., De Dachambre: Article "Ictere."

³² Quoted from Allbutt and Rolleston: System of Medicine, London, 1908, iv, pt. 1, 254.

³³ Ztschr. f. Heilk., 1893, xv, 199.

³⁴ Compt. rend. Soc. de biol., 1894.

³⁵ Bull. de la Soc. anat. de Paris, 1898, No. 12.

³⁶ Quoted from Allbutt and Rolleston: System of Medicine, London, 1908, iv, pt. 1, 254.

³⁷ Quoted from Allbutt and Rolleston: System of Medicine, London, 1908, iv, pt. 1, 254.

³⁸ Jour. Inf. Dis., 1916, xix, 527.

it to say here that a hypercholesterinemic condition may appear in the body economy, less frequently having its inception in some pathological disturbance of the normal metabolic activity, much more frequently owing to its origin to temporary, and apparently, necessary changes of the normal functions accompanying the physiological period of pregnancy. These disturbances may be repeated from time to time or may become continuous, and are found to precede or to be associated with the precipitation of stones in the biliary passages.

GALL-STONE FORMATION. Two theories have developed in regard to gall-stone formation. The one, sponsored by Naunyn³⁹ and his pupils Jankau⁴⁰ and Thomas⁴¹ has dominated experimental work for many years. Their work was done on dogs with biliary fistulae and resulted in the formation of the following theory: The cholesterin content of the bile is constant and independent of the blood and diet cholesterin. The cholesterin of the bile does not result from the general metabolism and is no specific secretion product of the liver. The cholesterin in the bile is derived from the epithelium of the gall-bladder brought about by a "stein-bildende Katarrh," and is initiated by bacterial infection. Naunyn found that in catarrhal bronchitis the cholesterin content of the sputum was 0.9 per thousand and in putrid bronchitis 1.5 per 1000 c.c. He assumed similarities in the pathological processes of catarrhal inflammations of all mucous membranes, attempted to show that an increased formation of cholesterin accompanies all of these inflammatory conditions and found in this conception the chief underlying factor in gall-stone formations. The presence of various organisms in the centers of the stones as well as in the gall-bladder wall lent support to this hypothesis.

Lichtwitz,⁴² in a recent critical review of the literature, concludes that at present we have no evidence of any interrelationship between blood and bile cholesterin. Since his time, however, both the work of other investigators and unpublished work of our own have definitely proved this relationship.

This relationship is the main support of the tenets of the opposite group. Aschoff and Bacmeister,⁴³ were the first to point out that, morphologically, those gall-bladders in which pure cholesterin stones were found show practically no inflammatory reaction. On the basis of this and some experimental work they advocated an "aseptic cholelithiasis" and advanced the theory of the cholesterin diathesis. The experimental basis for their theory is inconclusive, as it is necessary to prove a relationship between the cholesterin content of food, blood and bile.

³⁹ Klinik der Cholelithiasis, Leipzig, 1892.

⁴⁰ Arch. f. exper. Path. u. Pharmakol., xxxix.

⁴¹ Inaug. Diss., Strassburg, 1890.

⁴² Ueber die bildung des Harn- und Gallensteine, Berlin, 1914.

⁴³ Der Cholelithiasis, Jena, 1909.

Von Renvers,⁴⁴ from a purely clinical view-point, believed that an aseptic as well as a bacterial cholelithiasis existed. No laboratory evidence was given to support this view.

DISCUSSION. Assuming as our premise that the bile is a composite solution in which the cholesterin is held in a colloidal state, it follows readily that if simple precipitation occur the quantitative analysis of the stones found would reflect comparatively accurately the relative proportions of the solid substances in the bile. This would be true only in the event that no extraneous factor had been added which would tend to disturb the normal equilibrium. The actual state of affairs is demonstrated in the following classification, made from a quantitative chemical stand-point, of the stones examined in our laboratory. It is shown that there are:

1. Practically pure cholesterin stones. These average from 98 per cent. to 75 per cent. of pure cholesterin. We have considered this type as demonstrating the precipitation theory in accordance with the views of Aschoff.

2. Stones containing from 75 per cent. to 40 per cent. of cholesterin (layered stones), which we consider as having been formed in a bile partially saturated with cholesterin to which some extraneous factor has been added. These stones may be formed secondarily from stones originally belonging to the first group.

3. Stones containing from 40 per cent. to 5 per cent. of cholesterin. These stones are the small faceted stones with nuclei containing bile salts and some cholesterin and an outer shell usually consisting of pure cholesterin. These stones are infectious in origin. However, their formation may follow previously existing stones belonging to the first two groups.

4. Bilirubin-calcium stones. These stones are rarely found in the gall-bladder, much more frequently in the intrahepatic ducts and occasionally in the common bile duct. Practically all of the stones found in the cases of intrahepatic cholelithiasis are of this nature. These stones may have an infectious origin or may be formed by an increase in the bile of the precipitated substance. The cholangitis which usually coexists can be considered either as a primary or secondary factor.

Clinical knowledge supplies several of those extraneous factors which tend to disturb the normal proportions of the bile ingredients. These are:

1. Infection. Catarrh in the Naunyn sense would add from the exudate a higher quantity of cholesterin. The amount added, however, would form a relatively small porportion of the total. In other varieties changes in electrochemical potential might conceivably cause a precipitation.

2. Stagnation in the bile passages produced either by inflammatory stricture at any point of the duct system or by impaction of a previously formed stone.

⁴⁴ Ther. d. Gegenwart, 1908, No. 3.

In addition the studies detailed above have shown intimate relationships between food, blood and bile, which may be summarized as follows:

(a) The cholesterin content of the blood of various animals and human races depend on the cholesterin content of the food.

(b) The cholesterin content of the bile is dependent upon the cholesterin content of the blood.

(c) A marked increase of the cholesterin content of the blood will cause a marked increase in the cholesterin content of the bile. The converse of this is also true.

It is therefore possible to add another extraneous factor:

3. Hypercholesterinemic conditions in the blood.

The natural history of gall-stone formation goes to show that cholelithiasis is specially common in women who have been pregnant and among the people of the western part of the world who have omnivorous dietary habits. In those races studied by de Langen,⁴⁵ whose habits of life as regards food ally them to the herbivorous class, it is known that cholelithiasis is extremely rare. This phenomenon has been commented upon by the early English physicians and was confirmed by de Langen.⁴⁶ The latter also points out that when stone formation does occur in these people the calculi are almost always of the bilirubin-calcium variety and rarely of the cholesterin type. The relation between the low blood cholesterin contents and a comparative rarity of gall-stones is most significant.

Among the people of the western part of the world the great frequency of calculous formation in women is associated with the occurrence of pregnancy. During this physiological epoch the cholesterin content of the blood is continuously high and the hypercholesterinemia is protracted for a variable length of time after the birth of the child. It is common clinical knowledge that the first attack of gall-stone colic often takes place during the pregnancy or puerperium or a short time immediately thereafter.

When gall-bladder disease is found to affect men the clinical picture is frequently dominated by the evidences of bacterial infection and the finding of stones in the gall-bladder or bile passages is a secondary factor. Frequently, indeed, no stones are found.

It is not possible to ignore the significant and constant relationships outlined in this communication between the food, the blood and the bile, nor to accept as pure coincidences the association of abnormally high cholesterin contents of these three factors with the occurrence of gall-stones. The fact that in most of the cases the bacterial element, either primarily or secondarily, seems to dominate the clinical picture gives to it an undue prominence. Far better that we recognize the importance of the metabolic element in the pathological picture. Only then will it assume its proper place as one of the criteria upon which rational treatment can be founded.

⁴⁵ Loc. cit.

⁴⁶ Loc. cit.

SOME CLINICAL OBSERVATIONS ON THE LINGUAL TONSIL,
CONCERNING GOITRE, GLOSSODYNIA AND
FOCAL INFECTION.¹

BY GREENFIELD SLUDER, M.D.,

CLINICAL PROFESSOR AND DIRECTOR OF THE NOSE AND THROAT DEPARTMENT,
WASHINGTON UNIVERSITY MEDICAL SCHOOL, ST. LOUIS, MISSOURI.

ANATOMICAL observation and description of the lingual tonsil was given by Wharton,² Morgani,³ and Koelliker.⁴ Stoehr⁵ gave its embryological development and histology in 1891.

The first clinical observation concerning it was recorded by David Craigie⁶ under the title of "lingual quinsy," according to Sir Henry Butlin.⁷ Since that date a considerable time seems to have elapsed in which no observations on it are recorded. Clinical record of it begins again with McBride,⁸ Curtis⁹ and Swain¹⁰ (1884-1887), and since then it has made up a considerable literature; but even now this is very little compared with the writings upon the faucial or pharyngeal tonsils. This would argue its neglect or oversight by many observers who have contributed so much upon the other tonsils. This neglect is further emphasized by the very small consideration it has received from text-book writers.

It seems to me the lingual tonsil plays a far greater and more variegated part in the practice of laryngology than is generally thought. It is probably the most frequent clinical issue in the adult throat.

In my experience acute follicular lingual tonsillitis is not an infrequent accompaniment of acute follicular faucial tonsillitis in old or young, but is, however, overlooked unless the examination be made with the laryngeal mirror. In patients who have had the faucial tonsils enucleated it may replace the acute faucial tonsillitis, but is liable to be less frequently recurrent. Lingual quinsy is rare. The evidence of the acute lesion is striking, *e. g.*, dysphagia, fever, redness and swelling of the mass at the base of the tongue, with or without white or yellow spots marking the openings of the follicles. As the acute process subsides a widely variegated picture may follow and endure apparently forever.

¹ Read before the American Laryngological Association.

² Died 1763.

⁴ *Entwickillungsgeschicke*, 1876, 2 Auf.

⁵ *Festschrift*, Naegali u. Koelliker, 1891.

⁶ *Edinburgh Med. and Surg. Jour.*, 1834.

⁷ *Diseases of the Tongue*, 1900.

⁸ *Adenoid Tissue at the Base of the Tongue*, *Med. and Surg. Soc.*, Edinburgh, July, 1887.

⁹ *Influence Exerted on the Singing Voice by Glandular Hypertrophy at the Base of the Tongue*, *New York Med. Jour.*, 1884.

¹⁰ *Deutsch. Arch. f. klin. Med.*, 1886, xxxix, 504.

³ Died 1771.

Conspicuous in the symptoms of the subacute or chronic lesion is the sense of mucus in the throat with or without swelling of the mass. There may be mucus actually, but frequently only the sensation which "cannot be cleared away by either up- or down-going efforts." This sensation, moreover, is often wrongly placed by the patient. Many times I have known the most intelligent patients to refer it to the nasopharynx and vigorously maintain they had to "clear something" out of the back of the nose. And I have known such patients treated for many years for "nasopharyngitis." The reference of the sensation into the larynx is more frequent.

The sensation of pain in chronic cases is less frequent. In the subacute ones it may be present and located correctly or referred to the ear. It may be sharp on swallowing or be a sense of general stiffness, and may exist with much of the local appearance (redness and swelling) absent. Such cases often pass as gouty or rheumatic throats. I have, however, never found a "gouty" throat with the lingual tonsil *normal*, and they have been uniformly relieved by local treatment of the lingual tonsil. I have seen such a painful throat translated as caused by the "small embedded" faucial tonsil. It is, of course, disappointing to patient and surgeon when a perfect faucial tonsillectomy fails to relieve these symptoms. The sensation of a foreign body is often described as "a lump over which my throat must jump in order to swallow." Allied to this is the sensation described by patients as "falling of the palate" or "elongation of the uvula." The uvula under these conditions may or may not be a little longer than normal.

The globus hystericus of classical description may exist. Most cases of this phenomenon, however, in my experience have been acute or chronic tonsillitis in easily excitable or "nervous" people. This was also the observation of H. L. Swain in 1886.¹¹

Cough is a frequent manifestation of all grades of lingual tonsillitis. Particularly annoying is that accompanied by a sense of a feather tickling in the throat, which wakes the patient out of sleep, combined often with choking. It may possibly arise from contact of the enlarged tonsil with the epiglottis. It may be excited by laughing. The cough may be of any degree or duration. In the acute cases it may be intensely painful because the expired blast of air pounds upon the inflamed mass from below.

The veins of the lingual tonsil are a frequent point of bleeding in hemorrhage from the throat.

Enlargement of the mass may push the epiglottis down, causing strangling in sleep should the tongue fall back even to the slightest degree.

The singing voice is frequently disturbed by or lost because of

¹¹ Loc. cit.

lingual tonsillitis. The complaint is frequently that "I am uncertain of my tone," "I sharp or flat," which is what singers often refer to as bad "placing." Attention was called to this fact by Holbrook Curtis, 1884.¹² It is also very destructive to the durability of the voice for singers or speakers. They can sing or speak for a few minutes only when the voice gives way or cracks. This may happen because of the "stiffness of the throat," or because of the vulnerability of this inflamed district. It will not stand the work put upon it by such extra efforts. It is easily irritated and becomes uncomfortable or painful. The faucial tonsils are far less often the cause of or even party to these disturbances (at least in my opinion).

As a possible place of focal infection with systemic manifestations, the lingual tonsil should be quite as carefully and as seriously investigated and considered as the faucial tonsils. I have often seen it reestablish the systemic condition "rheumatism" for which the faucial tonsils had been enucleated, and I have seen that condition relieved by treatment of the lingual tonsil without the enucleation of the faucial tonsils.

As a factor in thyroid gland disturbances the lingual tonsil had not been recorded prior to my mention of it while discussing Dr. Shurley's paper before this Association in 1912. Seven years ago I saw in one of my own children (aged four years) the right lobe of the thyroid swell (to what appeared to be 50 per cent.) as an accompaniment of an acute follicular lingual tonsillitis. The sore throat was only six hours old, more marked on the right side. She had never had tonsillitis of any sort before nor any disturbance of the thyroid. It behaved like the glands in the neck with faucial tonsillitis. The lingual tonsil and thyroid were apparently normal again in ten days. The association of the thyroid, with the faucial tonsillitis, was called to our attention by Dr. Theisen in 1904 and Dr. Shurley in 1912. With my associate, Dr. C. A. Gundelach, in the St. Louis Children's Hospital, I have frequently seen this combination in children for whom the faucial tonsils had been enucleated long before. The clinical observation of this combination has been verified in adults by my associates, Drs. H. E. Miller, C. H. Bardenheier, W. M. C. Bryan, M. F. Arbuckle and H. B. Miller. I know of no explanation to offer for it. The lymphatics of the lingual tonsil are not known. In early fetal life an association of the thyroid with the base of the tongue exists. This was described by Bochdelag¹³ and His¹⁴ as the thyroglossal tract. Sir Henry Butlin¹⁵ thinks this explains the anomalously placed thyroid masses along this tract which are sometimes met with. But he does not think that a thyroglossal duct has been proved in the

¹² Loc. cit.

¹³ Oesterr. Ztschr. f. prakt. Heilk., 1886, xii, 683 et seq.

¹⁴ Arch. f. Anat. v. Physiol., Anat. Abth., 1891, 26.

¹⁵ Loc. cit.

adult. In an unsuccessful effort to prove a lymphatic connection, Dr. Gundelach and I have made a number of experiments, painting the tonsil with India ink for two weeks prior to the removal of goitres of various kinds. The thyroids did not show the ink. It is an inoffensive procedure and patients do not object to it, but we have not had a longer chance than two weeks. Were it prolonged into months it might answer better. We have also injected ink into the thyroid of guinea-pigs and dogs but failed to find it transferred to the lingual tonsil. But this clinical combination, together with the satisfactory results of treatment, make me feel this report to be justifiable.

In cases of thyroid enlargement of moderate grades of almost any duration it has proved helpful to treat the lingual tonsil even though it appeared normal. (As a fact, however, it very seldom has been normal. Often one lobe of the thyroid has been larger with a more marked lesion of the lingual tonsil of that side.) The goitre becomes softer and then smaller. These cases are frequently accompanied by a low or moderate hyperthyroidism. This also is much relieved or cured. The sense of strength and endurance of the patient rises rapidly. Indeed, hyperthyroidism may exist without external enlargement. In these cases the result of treatment is even more satisfactory, and in the few exophthalmic cases that I have had the opportunity of observing some were much helped and one case was cured. The goitre and exophthalmos shrank rapidly. The weakness, nervousness, tremor and frequent pulse were relieved. The case was apparently cured and has remained so for four years. It had lasted one year when treatment of the lingual tonsillitis was begun. It was six months in treatment, consisting of small applications of saturated silver nitrate to the lingual tonsil two or three times a week.

It is self-evident that cystic degeneration of the thyroid will not be helped by treatment of the lingual tonsil. Sometimes, however, one is surprised to see an old, hard, fibrous enlargement soften and diminish somewhat under such treatment. For the worst cases thyroidectomy must serve.

As a factor in painful tongue, lingual tonsillitis has seemed to me to play a causative part. This distressing condition is described by Sir Henry Butlin¹⁶ as glossodynia, and he calls attention to the fact that the papilla at the junction of the palatoglossal fold with the tongue is very frequently inflamed in these cases. It seemed to be a part of the syndrome. No explanation for this can be offered at present. Many times I have seen this papilla involved, with pain in the tip of the tongue as a part of a lingual tonsillitis, and remain so many months after the attack in the tonsil had disappeared. The lymphoid tissue of the tonsil often extends to this

¹⁶ Loc. cit.

point. Recently I saw these papillæ take part in the reaction from a galvanocautery destruction of the mass at the lowermost part of the lymphoid tissue at the base of the tongue 1 cm. to each side of the middle line.

DIAGNOSIS. The diagnosis of lingual tonsillitis is simple in acute follicular cases. Should it not assume the follicular markings it is often overlooked, particularly when the mass is not enlarged. It is recognized under these conditions by its color alone. The mass may be much enlarged in acute or chronic cases, which is, of course easily recognizable. Not so easily interpreted is an occasional small slightly reddened follicle. These are often the origin of the symptoms.

PROGNOSIS. The prognosis for singers and speakers according to my experience should be guarded. A lingual tonsil which easily becomes a disturbing factor either from the work of singing or speaking or from infection must be considered most seriously. I do not believe that the singing or speaking voice can be developed to any great extent under these conditions.

TREATMENT. The treatment of lingual tonsillitis in the acute follicular stage is like that for the faucial tonsils under like conditions. For the subacute or chronic state, with or without enlargement, nothing has been so satisfactory as applications of a small amount of silver nitrate saturated in 50 per cent. glycerin. Salicylic acid saturated in 95 per cent. alcohol is helpful and does not taste so unpleasant. These may be made daily or as seldom as ten days. For the enlargement, galvanocautery destruction has seemed best. Myles's lingual tonsil guillotine also serves well. Hemorrhage following surgery of the lingual tonsil is more difficult to manage than any in the upper air passages. It is fortunately rare.

I am aware that many of these observations have been made and recorded in more or less this form. The association of lingual tonsillitis with thyroid gland disturbance, focal infection and with glossodynia I believe has not hitherto been recorded.

It is my interpretation of clinical laryngology that the lingual tonsil plays a major role. I am aware also that this is in opposition to the views of some of the most distinguished observers, notably Sir Henry Butlin, who expresses himself very clearly on this point.¹⁷ I believe, furthermore, that laryngologists share his views to a greater or lesser extent.

An extensive bibliography of this subject is found in Hymann's *Handbuch d. Laryngologie*, Band ii, S. 638, "Die Krankheiten d. Zungentonsille," von J. Michael.

¹⁷ Loc. cit.

WAR MEDICINE

CONTRIBUTORS.

- LIEUTENANT-COLONEL SIMON FLEXNER, M.R.C., U. S. A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U. S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- COLONEL FREDERICK F. RUSSELL, M.C., U. S. A.
- DR. RICHARD M. PEARCE, National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, U. S. N. A.
- MAJOR R. M. YERKES, Sanitary Corps, U. S. A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- DR. E. E. SOUTHARD, Director of Psychopathic Department, Boston State Hospital.
- LIEUTENANT-COLONEL WARFIELD T. LONGCOPE, U. S. N. A. (Prof. Practice of Medicine, Columbia University).
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- DR. A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- LIEUTENANT O. H. PERRY PEPPER, M.R.C., U. S. A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Prof. of Pediatrics, Univ. of California).
- MAJOR FRED H. ALBEE, M.R.C., Director of Military Reconstruction Hospital No. 3, U. S. A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.R.C., U. S. A.
- DR. JOHN A. HARTWELL, Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- CAPTAIN RALPH PEMBERTON, M.R.C., U. S. A.
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

SURGICAL TREATMENT OF WAR WOUNDS.¹

By C. L. GIBSON, M.D.,

ATTENDING SURGEON, NEW YORK HOSPITAL.

As the present war has brought out entirely new military problems, so has the preconceived notion of treatment of wounds required entire revision. The wounds inflicted today are by new forms of projectiles, the supply of which in contrast to former methods is absolutely lavish. Deep trench warfare has rendered the soldier a filthy and constantly contaminated person, particularly the trenches of Flanders and Northern France, dug in soil which for centuries has been saturated with manure and other fertile sources of infection.

The treatment of war wounds is a highly specialized branch of surgery, and the rules of civil practice apply hardly, if at all, at the

¹ Read before the Medical Society of the State of New York, May 23, 1918.

front. Moreover, we have to deal with a different kind of individual than in civil practice. In the latter phase the factory hand who is badly hurt will, however, have been in good condition immediately prior to his injury, will have come from clean surroundings, his person and clothing will be relatively uncontaminated, will recently have had food and drink and will not have been exposed unduly, and perhaps for a long time, to the effects of cold and wet. When injured some form of competent relief is almost immediately at hand and transportation to a well-equipped hospital usually speedy and comfortable. Moreover, the treatment at this institution can usually be given promptly. The elements of fear and anxiety and the strain of prolonged expectation of injury are likewise absent.

The wounded soldier will probably have been subjected to harassing conditions of warfare. His injuries may be multiple. It may be some time before he is picked up and in addition to the other conditions he may be deprived of food and drink, especially the latter, for a long period of time. The journey out of the trenches is long, tedious, hazardous and may greatly add to the patient's shock. It is therefore obvious that special training for proper treatment of such cases must be obtained and must be derived from practical experience at the front and cannot be replaced by theory.

The three main factors of wounds are (1) shock, (2) hemorrhage and (3) sepsis. The latter element in this war is almost 100 per cent. possibility. Soon after the outbreak of hostilities it was generally conceded that this constant element of sepsis must be combated by something more than the usual line of treatment for every-day trauma.

In addition to laying open wounds freely, three things quickly developed, namely, the importance of early treatment, no matter what kind, the bad effects of leaving projectiles and other foreign bodies in the wounds, and the necessity of actual destruction of the bacteria. The first has been met by constantly moving up better organized lines of relief closer and closer to the front. At the present time it is aimed, if possible, to do such thorough and early surgery close to the lines that relatively little remains to be done at the rear. It becomes obvious that even by modern antiseptics no foreign body, usually contaminated as they are, could be sterilized by any method, no matter how efficient or thorough.

Credit is due to Dr. Carrel and his co-workers who have demonstrated that although bacteria can be very efficiently combated in the tissues at almost any stage, these methods fail in the presence of foreign bodies. Also proceeding on these lines it becomes evident that tissues which were damaged made favorable places for bacteria and were of themselves a source of danger.

It was pretty clearly demonstrated in 1916 by Carrel and some of those who followed his methods accurately, like Depage at LaPanne, that the Carrel method, providing the patient came under treat-

ment early and was submitted to thorough operation, namely, free excision of the tract of the missile and the removal of all foreign bodies, acted as an efficient prophylaxis against infection.

It will be appreciated that even with the demonstrated efficiency of chemical sterilization, good surgery applied at a very early stage was almost a *sine qua non*, and, in fact, chemical sterilization became an adjuvant and not a substitute for good surgery.

The Carrel method is well known or should be. In order to be efficient it must be done rightly. To be done rightly requires a series of steps requiring infinite care and continued treatment under the same conditions. It is quite impossible, under the unusual circumstances of warfare, to give the great bulk of wounded men who come to hospitals near the lines in large numbers, and in a short space of time, such treatment.

The present-day generally accepted method as practised by the Allies on the Western Front aims at prophylaxis of wound infection by a method which, in some ways, is simple, and if it can be carried out efficiently gives such good results as to minimize the necessity of complicated or prolonged after-treatment. The present-day method aims at the radical excision of all open wounds, removal so far as feasible of all foreign bodies, be they what they may, and the complete removal of all bruised, infiltrated, damaged or "shocked" tissue. Operations done on this principle and done thoroughly by highly competent surgeons, with a large experience in this particular line of work, give the surest guarantee against the development of all forms of sepsis, particularly the dreaded gas gangrene.

It has been my privilege to observe the workings of this method in both the British and French Armies. The principles in both armies are about the same, varying only in minor degrees and particularly in those of organization. This radical excision of wounds is usually done in the British Army in the so-called "Casualty Clearing Station," which will be situated ordinarily from five to ten miles back of the lines.

The wounded soldier is first brought to a dugout back of the trenches where first aid is administered and then to the dressing station, say one to three miles back of the lines at the end of the communication trenches, at a place where ambulances, motor or horse, can come with comparative safety.

The casualty clearing stations are mostly under canvas. Their units can be multiplied readily. In so-called "peace" times they have approximately 200 beds and a medical staff of 6, which can be increased to 800 or more beds and a medical staff of approximately 25. The patient is brought in carefully warmed ambulances, usually under a sufficient amount of anodyne to diminish shock, both physical and psychical. He is carefully unloaded in a waiting room which is well warmed and protected from drafts and passes

into an examining room when his wound and condition are carefully investigated by a highly trained and competent physician who decides on the various steps he will need.

A very few cases of apparently simple conditions may be transferred directly to a base hospital from the casualty clearing station, but the majority of the cases will need some form of operative procedure. The minor cases which form a large group are handled by a special surgeon and a special department and their conditions taken care of either with or without a local anesthetic or with "laughing gas." A certain group of cases may require operation, but their conditions are so precarious that it must be postponed until the patient can be brought back into better condition. These are sent to a special department, called the Resuscitation Ward, where they receive special attention and where there are special resources. Emphasis is placed on heat, particularly heat as given in hot-air baths. The administration of fluid is important as the dehydration of these patients add to the gravity of their conditions. When these patients seem in a condition to stand operation they are returned to the "pre op room," where all the patients await their turn to go into the operating room. Patients requiring an operation which is perhaps not very urgent may wait in the "pre op room" several hours, giving precedence to the more urgent cases. The patient is still kept very warm and is cleaned up to the extent his condition will allow. Badly shocked patients are little disturbed, their clothing being removed on the operating table when they are anesthetized. When the patient comes to the operating theater he is operated on by the surgeon, the head of the surgical team.

A surgical team consists of an operating surgeon of recognized capacity, a physician who acts as anesthetist and at other times does work around the hospital, particularly in the after-care of patients, a nursing sister who acts as assistant surgeon and instrument nurse and a trained orderly. These teams, which generally have been working together for many months, make for the highest efficiency and organization. These teams now bring with them a portable operating table and a supply of routine instruments. This system allows the localization of both personnel and apparatus when it is needed and under most economical management.

The English group their major operating in one single operating theater. This system makes for distinct economy of space and equipment and I have never seen any evidence of confusion arising from this method. (This plan is in contrast to the French system in which each surgeon has his own cramped and very small operating room.) The patients are, for the most part, given a general anesthetic, having already received in transit a generous supply of morphin. The skin is disinfected by mechanical cleansing with soap and water and 5 per cent. alcoholic picric acid solution, which is very efficient and non-irritating.

The surgeon is guided also in some cases by roentgen-ray pictures. In times of greater activity many roentgen-ray examinations have to be omitted and it is only in "peace" times that an appreciable amount of plates can be made, the patient having to be examined under the fluoroscope. The French have developed their fluoroscopy and other means of foreign body localization to perhaps a higher degree than the British and seemed supplied with rather better material resources.

The operation having been conducted along the lines already stated, it is customary in both armies to swab out the wound with some form of antiseptic, the most popular being ether, why, I do not know. Rather small and superficial lesions can be sewed up like ordinary operative wounds, but in the British Army the deeper wounds are more likely to be packed with gauze soaked in paraffin oil containing some form of antiseptic. One per cent. iodoform seems to be the most popular.

These patients are then returned to the wards, most of them to be evacuated on the first hospital train if their condition permits. While it is the aim of the casualty clearing station to evacuate patients for military and psychological reasons as soon as possible, it is generally planned to keep head, chest and abdominal cases one week.

At the base, wounds are redressed and packing removed at a varying time, usually on the average from five to six days. It is stated that the condition of the wound then allows of early suturing in layers and that the results are generally good. I have no means of corroborating this statement from personal experience, but I believe it to be true.

In the French Army primary suture of these wounds is done rather more freely than in similar institutions of the British Army and considerable reliance is placed on cultures; but if the culture shows a streptococcus or *Bacillus perfringens* the wound is immediately laid wide open and treatment of the open wound is instituted, either by the Carrel method or some other method as the operator practices.

With the French Army this means a somewhat closer relation between the H. O. E. (Evacuation Hospital) and the bases. Moreover, the French, so far as possible, like to have the base hospitals in which the work is to be continued only a relatively short distance away. It is the belief of the best surgical minds in France that a hospital situated at a point farther away than 40 to 60 km. does not really perform the function of an acute hospital but rather that of a convalescent home.

I deem it inexpedient to go further into the treatment of war wounds when they have been transferred in the later stages to the base hospital. The farther away from the front and the longer the time that elapses from the injury, more do the conditions resemble those of civil practice, and it is not my purpose to enter into consideration of these.

I recommend a pamphlet entitled "Surgical Treatment of War Wounds, in the Medical Units of the Third Army, British Expeditionary Force, with Special Reference to Casualty Clearing Stations, February, 1917," which gives thoroughly and more in detail some of the points I have touched on in this article. I append two articles from this pamphlet:

RECEPTION AND DISTRIBUTION OF CASES IN A CASUALTY CLEARING STATION.

BY CAPTAIN E. W. N. WOOLER, R. A. M. C.

RECEPTION OF CASES. On arrival, patients are sent to the reception room or rooms. If only one is available it is partitioned so that lying cases go to one side of the partition, walking cases to the other. It is better, however, to have separate huts for each class. Their names are entered in admission and discharge books. They are then sent to separate dressing rooms, one for lying cases and one for sitting cases. In case of a big rush, accommodations for 100 to 200 cases or more should be available near the reception huts, where patients may be put before their names can be taken. This prevents the ambulance cars being held up unduly.

Dressing Room. The dressing room for lying cases should have accommodation for about 8 cases on folding tables at one time. These wooden tables should be substantial, and are made in such a way that when the stretchers are placed on them the poles of the stretchers fall over the sides of the tables and so facilitate the dressing of patients. They are arranged in two rows of four, each of the two medical officers on duty dealing with the cases in one row.

Annexe. A part of each dressing room is screened off to form an annexe for the performance of minor operations.

DISTRIBUTION FROM DRESSING ROOMS. A. *Lying Cases.* All cases fit to be evacuated to the base forthwith are sent to marquees or huts, where they are fed and otherwise attended to until a train is available.

The following is a rough classification of those cases which are detained:

1. *Abdominal Cases.* Abdominal cases in which penetration of the abdomen is suspected. Wounds of the chest, especially of the lower part, of the lumbar region, sacrum or buttocks should always lead one to examine carefully for abdominal symptoms.

2. *Chest Cases.* Chest cases in which penetration of the chest is evident from the urgent symptoms present. Other cases in which penetration is merely suspected or very doubtful can be evacuated at once.

3. *Head Cases.* A large proportion of head cases, namely, those with "compression" symptoms or which show undoubted evidence

of injury to the brain, especially if brain matter is exuding from the wound.

4. *Gas Gangrene.* Cases of gas-infected or suspected gas-infected wounds, *e. g.*, a limb showing tension even though there is no evidence of actual gas formation.

5. *Femur.* Cases of compound fracture of the femur and all other fractures which cannot be thoroughly cleaned up and efficiently splinted in the dressing room.

6. *Oozing.* Cases of deep-seated hemorrhage, even though the vessel concerned is not a large one. Many men arrive in an exsanguine condition, owing to their wounds having oozed steadily all the way down; but the appearance of the wound at previous dressings has not led each succeeding M. O. to attach much importance to it. By the time the man arrives at the casualty clearing station he has lost quite a considerable amount of blood.

7. *Shock, External Hemorrhage.* All cases suffering from shock, external hemorrhage, etc., unfit for evacuation, whether cases of above types or not, *e. g.*, cases of multiple wounds.

8. *Flesh Wounds.* A variety of flesh wounds which do not admit of immediate evacuation, or which cannot be dealt with in the operating annexe, *e. g.*, a limb showing a large wound (but no fracture), with considerable destruction of muscle tissue. The extent of operation required may be beyond the limits of the annexe with gas anesthesia, and the case should therefore be sent to the theater.

DISPOSAL OF CASES. 1. *Abdominal Cases,* if fit for immediate operation, are sent to the preoperation room for preparation. If unfit for operation at the time of admission, they are sent to the ward set apart for resuscitation of cases, or to the special abdominal ward.

2. *Chest Cases.* Chest cases are sent to wards set apart for them.

3. *Head Cases.* Head cases are sent to the preoperation room.

4. *Gas-infected Wounds.* Cases of gas-infected wounds are sent to the preoperation room.

5. *Compound Fracture of the Femur.* These cases as well as some other fractures are sent to the preoperation room.

6. *Hemorrhage.* Cases of deep-seated hemorrhage are sent to the preoperation room.

7. *Flesh Wounds.* Cases of flesh wounds are sent to the preoperation room.

8. *Shock, etc.* Cases suffering from shock or effects of severe hemorrhage are sent to the resuscitation wards.

The M. O. in charge of these wards (preoperation, chest, and resuscitation) notifies the surgeon-in-charge as soon as a case is fit for operation or develops symptoms necessitating immediate operation. Cases suffering from active hemorrhage which cannot be dealt with in the dressing room should be notified to the surgeon-in-charge of the theater at once.

GENERAL PRINCIPLES GUIDING THE M. O. IN DECIDING WHETHER TO EVACUATE OR DETAIN A CASE. 1. If there is any tension, edema or inflammation around the wound.

2. The presence of a thin brownish discharge which exudes under pressure.

3. An odor "fecal" in character.

4. If the wound is one in which gas-infection is likely to develop if left alone, *e. g.*, a small wound of entrance which has become wholly or partially occluded and in which there is much laceration of deeper parts.

If the condition of a wound is satisfactory and presents none of these appearances or if its condition can be dealt with in the operating annexe, such a case may be evacuated. The presence of any one or more of these phenomena, which is outside the scope of the annexe, should lead to the case being detained and sent to the theater.

5. Some cases which have been lying out for several days and are suffering from the effects of exposure and starvation should be detained, although their wounds might admit of their being evacuated.

6. Finally, attention must be paid to the number of cases accumulating for the theater, and should that number become large—say 40 or over—cases may have to be evacuated which would otherwise, for the sake of safety, be sent to the theater. Their wounds should be opened up by well-placed incisions. This can sometimes be done without anesthesia, *e. g.*, in a transverse wound, by incision on the distal side where the nerve supply has been cut off.

ANNEXE TO DRESSING ROOM. This consists of a part of the dressing room, screened off and fitted up for the performance of minor operations under gas or ethyl chloride anesthesia. By having such an annexe the theater, which is always working at high pressure, is relieved of a certain amount of operative work, and the routine work of the dressing room is thus interfered with less than if operations are carried out in it. There is also the additional advantage that other men do not see anesthetics being given nor operations being carried out.

TYPE OF CASE AND EXTENT OF OPERATION SUITABLE FOR OPERATING ANNEXE. 1. Cases of gunshot wound in which a foreign body can either be felt or seen projecting beneath the skin and which can be easily removed. When, *e. g.*, abdomen or joint is implicated, such cases *must* go to the theater.

2. Cases of gunshot wound in which enlargement of the wound will afford better drainage and lessen the risk of the wound becoming occluded and developing a gas infection.

3. "Simple," in the strict sense of the term, as opposed to "compound" fractures, *e. g.*, of the femur, for application of a Thomas splint.

4. All cases of compound fracture which require redressing and reapplication of the same or another type of splint, but which do not call for immediate theater treatment. This only applies to cases in which the wound is freely open and there is no great comminution of bone as all severe compound fractures should be sent to the theater.

5. Lastly, if the pressure on the theater is great, a few cases in which a limb is practically severed may be dealt with and amputation completed, provided other considerations, such as the general condition of the patient, admit of this procedure. As the stumps in most of these cases will require extensive trimming, amputation is not recommended for the annexe except under conditions of extreme pressure.

Following the administration of gas, etc., cases should be detained in the annexe for a quarter of an hour before being sent to the evacuation shelters. This principle is of more importance with reference to cases which have received theater treatment and are suitable for evacuations.

ORDINARY CASES WHICH SHOULD BE "TAKEN DOWN" WITHOUT FAIL IN THE DRESSING ROOM. 1. When dressings are soaked with blood.

2. When splints are not applied properly or when unsuitable splints have been used.

3. When swelling has occurred, particularly in distal parts of limbs, which may indicate "concealed" hemorrhage.

4. When genuine complaints of much pain are made, especially if of recent development, possibly indicating a gas infection.

5. Every case of gunshot wound of the head. Many cases with severe fracture and with brain matter exuding *walk* into the dressing room.

SCHEME OF LABELING. In the distribution of lying cases from the dressing room it is necessary to employ some scheme of labeling in order to avoid confusion. The larger proportion of cases will be found fit for evacuation (probably about three-quarters), and these are marked with a red label bearing the letter "E." Other cases are labeled with a label, the color differing according to whether the case is intended for chest wards, preoperation room or resuscitation wards, etc., each label bearing the name of the ward in addition. By combining the name of ward with a distinctive color, there should be no mistake on the part of the stretcher-bearers as to the allocation of a case. Except in the case of red "E" labels, the numbers of which must be unlimited, the number of other labels for chest and resuscitation wards should correspond to the number of beds available in each ward. The labels are sent back to the dressing rooms as the patients are evacuated and are kept there in a special box for each sort. In this way the M. O. knows when such a ward is full. By checking the number of labels issued for the preoperation room

an indication of the amount of work awaiting the theater staff can be obtained.

Walking Cases. In dealing with "walking cases" the same general principles are followed as with the lying cases and the same scheme of labeling is employed.

A small operating annexe for minor operations is also screened off for the same type of case and with the same scope of operation as in the lying cases.

CASES FOR EVACUATION FROM THE DRESSING ROOMS are sent, "sitters" to a large shelter, lying cases to special marquees in the Evacuation Department, where they can be fed and otherwise attended to. Marquees are available also where sitting cases can go and lie down if they wish to, pending the time for their evacuation by train. If there is much delay, many of these cases will require dressing.

THE PREOPERATION ROOM. The preoperation room should be capable of holding at least 30 to 50 cases on stretchers. Every case for operation, except those mentioned above for special wards, passes through this room before going to the theater, and is undressed, shaved, etc. In this way the wards are spared a great deal of unnecessary work, as no case for operation, unless specially collapsed, etc., is taken to any ward until it leaves the theater. In addition the patients benefit by remaining on the stretchers until they are put on the table, and have not to be lifted from stretcher to bed, or *vice versa*.

SOME IMPRESSIONS GATHERED IN THE DRESSING ROOM. *Question of Frequency of Dressing.* A very large number of both lying and walking cases have been brought in which have been dressed at the regimental aid post, advanced dressing station, main dressing station, and, in some cases, finally at the corps dressing station, before reaching the casualty clearing station. On an average these dressings have been done during a period of six to twelve hours. So far as the walking cases are concerned, this appears a waste of time and of dressing material, and in lying cases, especially those severely wounded, is, in addition of very doubtful value from the point of view of the patient.

In order to lighten the work at a casualty clearing station it would be well to develop the work at main dressing stations in a more specialized way, *e. g.*, by having an experienced officer to select cases, serious ones, including all fractures, not requiring immediate attention, to be sent on at once to the casualty clearing station; lighter cases, likely to be able to travel to the base, to be carefully dressed and labeled in some way to indicate that they need not be dressed again at the casualty clearing station, whether labeled in this manner or not. It will be made evident, from the papers which are to be read, what points require special attention from M. O. S. in field ambulances, etc.

In a general way the rule should hold that no dressing should be changed unless there is some definite indication for it.

THE ARRANGEMENT OF WORK WHEN TWO OR MORE CASUALTY CLEARING STATIONS ARE WORKING IN CONJUNCTION. 1. *Each May Be on Duty for Twenty-four Hours at a Time.* This is most practicable in quiet times, but during an offensive one the casualty clearing station alone may not be able to deal with all the cases which may arrive in that period; and, again, it frequently happens that under this scheme one casualty clearing station is worked very hard for one period of twenty-four hours while the other is comparatively quiet in the succeeding twenty-four hours. Lastly, during a period of this length, cases for operation accumulate and many have to wait even until next day before they receive attention. The danger of gas gangrene developing under this system is evident.

2. *Each casualty clearing station* receives a definite number of cases (*e. g.*, 200) and is then relieved by the other. The disadvantages of this scheme are twofold. In the first place the receipt of 200 cases may not be any indication of the amount of work which has to be done. For instance, three-quarters of the 200 may be walking cases, and therefore the amount of operative work involved is light compared with that which may fall to the lot of the other casualty clearing station should their 200 be composed of a large proportion of lying cases. The danger of gas gangrene involved in the accumulation of cases and consequent delay in treatment is almost as great in this scheme as in the first.

3. *Each casualty clearing station* received a definite number of cars alternately (*e. g.*, six cars).

This scheme appears to have none of the disadvantages of the other two. The danger of gas gangrene through delay in treatment is greatly reduced and the work is divided evenly between the two units. A disadvantage may lie in the fact that both casualty clearing stations will be more or less on duty continuously, owing to the small number of cars taken by each, and therefore will never have a rest for long. But it is upon this small number that the efficiency of the scheme depends.

CONCLUSION. Such is the scheme I would recommend for the reception and distribution of cases, based on three months' experience of dealing with large numbers. The whole basis of the scheme depends upon one main factor—that of deciding in the dressing rooms what is to be done with each case as opposed to any other scheme whereby such decision is arrived at in the wards.

SOME PRINCIPLES OF TREATMENT OF GUNSHOT WOUNDS.

BY CAPTAIN C. H. UPCOTT, R. A. M. C.

After two and a half years of war there is still great divergence of opinion on the subject of wound treatment. This is partly due to the

fact that military necessities make it impossible for any one man to have cases under observation from the time when the first surgical treatment is undertaken until complete recovery. Many men have written lauding this or that form of treatment, but their observations refer only to a certain period in the history of a wound, and they are generally concerned with the powers of some particular chemical application to hasten the healing process. This quest of the healing balm continues, and, I think, obscures the one common point where all agree—the need for free enlargement of the wound. It is of this exteriorization of wounds that I wish to speak.

It must be understood that my remarks are confined to the work of a casualty clearing station, I have no other experience. I have been guided by the behavior of wounds during the few days the patients have remained in the casualty clearing station and by occasional reports from the base on the later progress of cases.

Most cases arrive at a casualty clearing station between six and twenty-four hours after the infliction of the wound, and, provided the patient's general condition permits of it, the sooner the wound is attended to the better. This proviso as to the condition of the patient raises one of the most difficult problems with which we have to deal. A patient arrives profoundly shocked by his wounds, the cold, and the superadded trauma of the journey. The usual methods for treating shock are applied: warmth, fluids, rest and the alleviation of pain.

Recently transfusion of whole blood has been widely advocated. While in some cases the immediate revivifying effect of this procedure is striking, in many the benefit appears to be no more than could be attributed to the bulk of fluid injected. In cases suffering from combined shock and hemorrhage it may be that the blood introduced merely goes to fill the venous pool of the relaxed abdominal vessels. Tight bandaging of the limbs or abdomen is always applicable and should be used in conjunction with transfusion. Apart from blood transfusion the subcutaneous or rectal infusion of saline or glucose remains our chief stand-by in the ward treatment of severe shock. The glucose issued in the form of powder appears to be infected with moulds and solutions made from it soon become turbid, even after sterilization. Indolent abscesses sometimes occur at the site of subcutaneous glucose solution, which may perhaps be attributed to this cause. In the early stages of anaërobic infection the intravenous infusion of sodium bicarbonate is of great value. As a stimulant in these cases a hypodermic injection of 10 minims of a 10 per cent. solution of camphor in olive oil should be given and repeated if necessary.

After a few hours there may be a slight improvement in the patient's general condition; then the symptoms of shock merge into those of an overwhelming toxemia suggestive of "acid intoxication." The pallor becomes more marked, the breathing more shallow and

often sighing, the feeble pulse, formerly imperceptible, becomes increasingly rapid, while the temperature remains low. The patient often vomits; his mind is alert, but there is little complaint of pain. These are the early signs of deeply spreading anaërobic infection, so liable to occur in wounds of the buttock or thigh, and unless an operation is performed promptly the patient will die. The difficulty lies in choosing the moment to stand an operation and before he has been weakened by the toxemia. I am accustomed to rely chiefly on the character of the pulse; as soon as it can be felt at the wrist a one- to two-hourly record of its rate should be kept, and if this shows a progressive speeding up you have an urgent indication for operation.

It is well to bear constantly in mind the state of affairs existing in a gunshot wound, and the objects to be attained by operation. A missile passing through a limb dissipates a considerable amount of its energy in the tissues; they are struck a terrific blow and the greater the resistance they offer the more energy will the projectile lose in its flight. When the resistance is enough to arrest, for example, a bullet, it is obvious that all the energy of the missile is spent in the body. It does not follow, however, that the tissue injury caused by a lodging wound is greater than that from a traversing wound; the special gravity of lodging wounds depends on other factors. Given an equal resistance to its passage, the higher the velocity of the projectile, the greater the damage inflicted on the tissues. And this damage is not limited to the track of the missile; it imparts its momentum to everything in its line of flight, so that a radiating area of vibration is set up destructive to cellular life. If the tissues vary in density, the more compact will be driven through the more yielding, with a slattering effect.

This is the first point of importance; the immediate destructive effect of a projectile is not limited to its path.

The second point is that practically every wound is permeated with foreign material bearing aërobic and anaërobic organisms, and some of the latter are capable of thriving in the devitalized tissues among which they are sown.

The object to be attained by operation is a widely open wound, from whose surfaces all foreign matter and dead tissue have been removed.

TYPES OF WOUNDS. The types of wounds are so manifold that any classification is difficult, but they may be placed in three groups, to provide headings for the discussion of treatment.

1. *Simple Perforating Wounds in Which the Track is of about the Same Diameter as the Skin Aperture.* An example of this group is a bullet traversing at long range the soft tissues of a limb. Entry and exit are small and the damage to muscle is slight.

The majority of these wounds require no operative treatment, or, at most, excision of skin and fascia. Depending probably on the

state of the muscle as regards contraction at the moment of impact, small entry and exit wounds are sometimes accompanied by great destruction of muscle; such cases belong to group 3.

Wounds caused by shrapnel balls have certain peculiar features. Here you have a smooth spherical projectile of low velocity. Having penetrated the skin, its smooth rounded surface enables it easily to find a passage through the muscles, often without causing much surrounding disturbance, but its velocity is so low that it is very frequently held up in meeting tissue of greater resistance. Indeed, it is remarkable how often shrapnel balls are found lodged beneath the skin after having perforated the body or a limb. If the ball and other foreign material are removed, and the entry wound excised, the track does not often cause trouble, although one would think that the wad of clothing carried in ahead of the ball would give rise to serious infection.

2. *Wound in Which the Destruction of Skin and Superficial Tissues is of Greater Extent than the Destruction of Deeper Tissues.* In such wounds as these (gutter wounds, explosive exits, superficial lacerations, avulsions) the wound is more or less exteriorized and all that is required is the excision of all the damaged tissue, in order to attain the ideal of an open wound with a living, uninfected surface.

If this can be assured, the new wound may be closed by primary suture, but unless one can be absolutely certain that the whole of the original wound surface and underlying "shocked" tissues have been removed without infecting the new wound, suture should not be attempted.

3. *Wounds in Which the Skin Aperture is Small in Relation to the Extent of Damage Inflicted on Deeper Structures.* Such wounds may be divided in: (a) lodging wounds; (b) traversing wounds.

This group includes the majority of wounds; and, apart from injury to important structures, these are the wounds that most urgently call for surgical treatment.

TECHNIC. 1. *Sterilization of the Skin.* Hairy parts should be shaved. If the skin is heavily caked with mud a scrub with soap and water is advisable; in most cases that may be omitted. Cleanse the skin by rubbing with swabs, wet with an antiseptic, such as Dakin's fluid or eusol, for two or three minutes; follow by rubbing with methylated spirit for one minute. During this process the surface of the wound should be covered with an absorbent swab, so that its discharge may not escape and soil the skin. With a pair of forceps, pack the wound with gauze dipped in 5 per cent. alcohol solution of picric acid (or 10 per cent. iodine).

In the case of a wound of group 3 this allows one to ascertain the direction of the track, a search that is often aided by moving the limb in different directions.

Finally, paint the skin with the picric solution and allow to dry while the towels are being placed in position. I have found that skin

treated thus can be rendered sterile. The process may often be carried out during the induction of anesthesia. Hurry and lack of method in cleaning the skin will result in failure to achieve sterility.

2. *Excision of Gutter Wound (Group 2)*. The raw surface of the wound is dried and repacked with gauze; it is then completely encircled by an elliptical incision, which should not be less than one-fourth inch from the edges of the wound. It is advisable to complete one side of the ellipse first, cutting deeply through skin and fascia together, and then deepening the cut rapidly until it has reached beneath the deepest part of the wound. This incision is then packed with gauze while the other half of the ellipse is made, so cutting out a wedge of tissue enclosing the wound and not opening into it at any part. The use of a finger in the wound sometimes enables one to cut clear of pockets which would otherwise be opened. If this be done the same finger should be kept in the wound until the excision is completed; it is then disinfected or the glove changed. All bleeding is carefully stopped and the wound closed with silk-worm-gut sutures, which should just emerge in the depth of the wound as they cross from side to side. Gum-mastic varnish, or better, "aëroplane dope," makes a good dressing, and the limb should be firmly bandaged to prevent effusion. If the original wound is opened into at any part during the operation, primary suture should not be done, but the edges may be lightly drawn together over a salt pack or the wound may be left open and sterilized by the Carrel-Dakin method.

3. *Excision of Traversing Wound with Explosive Exit (Group 2)*. Pack the wound firmly with gauze. Enter the knife vertically not less than one-quarter inch from the edge of the wound, and keeping the blade parallel with the sides of the wound, cut all the way around it, deepen the incision if needed until the apex of the wound is reached, thus making a cone-shaped excision of the wound. Dressing may be either a small central tube to the track of the missile surrounded by salt pack or by Carrel-Dakin.

4. *Tunnel Wounds (Group 3)*. Draw a strip of gauze through the tunnel and connect the entrance and exit wounds by an incision, cutting down on to the gauze, discard the soiled knife, and excise the wound as in 2. Narrow tunnel wounds should not have a rubber drainage tube drawn through them. This only blocks discharge, and if near a bloodvessel it is liable to cause ulceration of its walls.

5. *Traversing Shell Wounds (Group 3)*. Entry and exit should be excised by elliptical incisions. Usually it is unnecessary to excise more than one-quarter inch of skin around the wound. As a general rule the area of skin excised varies inversely with the skill of the surgeon. In doing this the knife should be plunged through the skin parallel to the track of the missile and an attempt made to excise the tissues around the wound to the depth of the knife blade in one piece. The crushed muscle and aponeurosis in the deeper parts of

the wound are seized with tissue forceps and cleanly excised. If sufficient access is not provided by the original wound excision the ends of the ellipse should be prolonged, so that the sides of the wound may be retracted. It is well to remember that prolonged and forcible retraction of muscle is liable to crush its tender fibers and render them a prey to saprophytes in the wound. The need for powerful retraction may be avoided by the use of free incisions. In dealing with the deeper parts of the wound it is to be remembered that the gravest danger arises from infection with gas-producing bacilli, which grow most readily in dead and dying muscle. The following points are important:

1. If a muscle is deprived of its blood supply it will not bleed when cut and will probably die.

2. A dead muscle will neither contract nor bleed when cut.

3. A muscle in the first stages of invasion by anaërobes (possibly when poisoned by toxine) loses its normal resilience and has a peculiar brick red color.

4. In the later stages of invasion the muscle becomes crepitant and exudes a dark reddish-brown foul-smelling fluid.

Taking singly the most important of these signs is absence of bleeding on section. A muscle may fail to contract when cut so that if this sign is present alone the muscle need not be excised.

6. *Lodging Shell Wounds (Group 3)*. These are to be dealt with on the same lines as 5 (traversing shell wounds), with the addition that every effort should be made to find and remove the shell fragment and any particles of clothing carried in with it. To this end exploration by sight is more valuable than by the sense of touch alone, whether roentgen-ray localization has been done or not. In these cases it is sometimes difficult to find the track of the missile. If the skin and fascial wound be excised and then the limb be removed, so that the muscles and skin assume different relative positions, the track will become visible and its direction may be gently explored with the finger and excised. In cases in which the metal fragment is lodged among pieces of bone in positions where the wound cannot be opened up I have found the Mackenzie-Davidson telephone probe of great service.

Lodging wounds often need a counter incision, either for the purpose of removing the projectile or to provide drainage. The objection to dependent drainage openings if the Carrel-Dakin treatment is to be adopted must, however, be borne in mind.

7. *Multiple Wounds*. These deserve separate mention on account of their frequency and by reason of the special problems they present. The condition of the patient often will not allow one to deal with each wound as thoroughly as could be wished. The first thing to do is to determine the general direction of the projectiles. A search will generally reveal a graze, a gutter or tunnel wound, giving a clue to the course of the others. It then remains to decide which

wounds should be first dealt with. Excluding fractures or penetration of the body cavities, lodging wounds of the buttocks, thighs, calves, shoulders and root of the neck should receive preference. If "time" presses, other wounds may be simply laid open by an assistant, and a salt tablet wrapped in wet gauze laid loosely in each.

HEMOSTASIS. At the conclusion of all these operations great care should be devoted to hemostasis, for pools of blood allowed to accumulate in the corners of the wound favor the progress of sepsis. Seeing that these wounds are accompanied by much crushing of tissue a plentiful supply of thrombokinase will be present, and once the larger vessels are secured, oozing may be stopped by pressure.

LOCAL REST. Local rest to the injured part is to be secured by firm dressings—and in this respect the salt pack is valuable—or by splints. The use of supporting splints should not be confined to fractures and joint injuries. Further, wounded muscles which have a large excursion on movement of neighboring joints, should be immobilized by fixing those joints.

AFTER-TREATMENT. In regard to the care of a wound after operation; although I know that sterility may be procured by the strict application of Carrel's methods, I am equally certain that these methods are not feasible during a heavy rush of work at a casualty clearing station, however satisfactory they may be in "peace" times.

I believe that for the majority of wounds, after correct operative treatment, the salt pack is the best dressing in times of pressure. But it must be carefully and exactly applied; a little extra time devoted to the proper application of the dressing is repaid by the absence of any further need for disturbance of the wound during the short time that the patient remains in the casualty clearing station. Wounds involving the main vessels of a limb, and fracture with much comminution, are not suitable for the typical salt pack.

I am fully conscious of the inadequacy of this paper; the subject involves so much tedious detail that the principle of wide excision has been ruthlessly applied in its preparation; but I have tried to lay stress on what I believe to be the most important part of the treatment of a wound—its early operative cleansing—without infringement on the subjects of those who are now to deal with regional surgery.

CEREBBOSPINAL FEVER.

BY FRANK MARINO, M.D.,

FIRST LIEUTENANT, M. R. C., MEDICAL SERVICE, BASE HOSPITAL, CAMP MEADE,
MARYLAND.

THERE have been 36 cases of cerebrospinal fever sent to the Base Hospital up to the date of writing, and the majority of these cases have conformed to well-recognized types. With a few, on the other hand, the clinical picture or the bacteriological study has been sufficiently unusual or new to deserve publication. The occurrence of primary septicemia in this disease is important in the bearing the fact may have upon the portal of entry of the infection. Some of the recent papers have accentuated this point¹ and cast some doubt upon the idea of infection of the meninges by direct extension.

The following cases are reported, with the consent of the Chief of the Medical Service, Major N. B. Foster.

CASE I.—Private G. A. B., of the 27th Engineers, entered the hospital on February 11, 1918, complaining of headaches. His past and family histories were negative. The patient had been enjoying good health until February 7, when he was taken with a sore throat. This was soon followed by violent frontal headache, pains in both legs and indefinite pains in the abdomen. The symptoms became progressively worse, and on February 11 he was admitted to the Base Hospital. On admission the patient was apparently in deep coma. There was marked opisthotonos, with stiff neck, positive Kernig and increased reflexes. His eyes were sunken, pupils dilated and reacted to light. The breathing was very irregular and apparently an atypical Cheyne-Stokes variety (Biot). Examination of the lungs was negative; heart was slightly dilated; sounds at both apex and base were very distant, weak and irregular. The abdomen, lower extremities and joints were negative.

The patient had a peculiar death-like cyanosis and the skin over the whole body was covered with a cold, clammy perspiration. Over the anterior surface of the neck the whole of the chest and abdomen and over the back are found innumerable purplish-blue hemorrhagic areas. They are not elevated above the skin surface and do not disappear on pressure. Pulses could not be felt. Temperature, 104°; respiration, 48. A blood culture was made immediately. Spinal puncture gave clear fluid under very slight pressure; negative globulin, cell count of 127 per cubic millimeter and a negative culture.

In spite of the negative spinal fluid findings the patient was given both intravenous and intraspinal antimeningococcus serum. The

¹ Herrick, W. W.: Arch. Int. Med., 1918, xxi, 541.

patient grew steadily worse and died about nine hours after admittance.

Clinical diagnosis: meningococcus septicemia and cerebrospinal meningitis.

Postmortem examination: scattered over the entire body are many macular hemorrhages, varying in size from just visible to about 5 mm. in diameter. There is marked congestion of the dura, with edema and intense hyperemia of the pia. There is a marked amount of fluid in the basal cistern. The lateral ventricles are filled with blood-stained fluid. The choroid plexus is intensely congested, with no pus collections. The spinal cord is negative except for congestion. Scattered throughout the peritoneum, pleura and pericardium, heart, lungs and liver are found many pin-point hemorrhages similar to those noted on the skin. Smears made from the cord showed many Gram-negative diplococci. No pus cells found. Blood culture reported twenty-four hours later is positive for meningococci.

Anatomical diagnosis: meningococcus septicemia and cerebrospinal meningitis.

CASE II.—Private J. G., of the 154th Depot Brigade, entered the hospital February 18, 1918, complaining of marked pain of the abdomen. His family and past history were negative. The patient began having headaches on February 17. This was soon followed by marked pain in the right iliac region, constipation, fever and tympanites.

On admission the patient was apparently suffering marked pain. The face was drawn, head and neck rigid, spine stiff, tongue coated, breath foul. Examination of the heart and lungs was negative. The abdomen was markedly distended and tender and rigid over the appendix. All the reflexes were exaggerated; Kernig and Brudzinski positive. Over the chest and abdomen were found a large number of irregular subcutaneous petechial hemorrhages, purplish blue in color, which did not disappear on pressure. A tentative diagnosis of spotted fever was made and a spinal puncture done immediately. Seventy cubic centimeters of a clear spinal fluid was removed, under marked pressure, containing 32 cells to the cubic millimeter; negative globulin and negative culture. In spite of the negative spinal fluid the patient was given 60 c.c. intraspinal, antimeningococcus serum. A blood culture was made and 60 c.c. of serum was given. About eight hours later the symptoms became more pronounced and the patient was again punctured and 35 c.c. of cloudy spinal fluid removed. This showed a positive globulin, 89 per cent. polymorphonuclear cells and positive cultures. The blood culture also showed meningococci.

February 19. Spinal puncture was done, 60 c.c. of cloudy fluid removed under marked pressure and 30 c.c. of serum given intraspinal and 40 c.c. intravenously. The temperature dropped from 104° to 99° and the patient was much improved.

February 20. Spinal puncture showed fluid under slight pressure and clear; 15 c.c. removed. No serum given intravenously. The patient's meningeal symptoms are markedly improved but abdominal symptoms are still present.

February 24. There are swelling, pain and definite evidence of inflammation in the left elbow and left knee. Conjunctiva of the right eye is inflamed and contained some pus. Temperature, 99°. Smears from the pus failed to show any meningococci.

February 25. The patient showed definite evidence of acute iritis of the right eye with slight cyclitis.

February 26. The right lens is opaque and there is complete loss of sight. There is still marked pain in the abdomen, with a tendency to tympanites. The right epididymis is slightly tender. There is no history or evidence of venereal disease.

February 28. The patient has developed a marked orchitis on the left side. Right knee now inflamed. Left knee shows definite evidence of fluid. Paracentesis of the left knee-joint reveals purulent fluid. Cultures negative. Patient now has pain in right hip.

March 1. There was 40 c.c. of purulent exudate removed from the left knee and 40 c.c. of serum given in the joint, also 40 c.c. given intravenously.

March 3. Fifty-five cubic centimeters of purulent exudate removed from the left knee and 40 c.c. of serum given in the joint, also 40 c.c. of serum given intravenously. Temperature, 98°. General condition improved. Swelling of the left knee has disappeared. The patient has good motion in this joint.

March 6. Thirty cubic centimeters of cloudy fluid removed from the left knee and 20 c.c. of serum given in the joint.

March 9. The knee has apparently cleared. Iritis and cyclitis improved, elbow- and knee-joints normal. The patient complains of occasional pain in the abdomen and pain in the right hip.

March 18. The patient has had a slight temperature up to 99.8° in the afternoon and complains of pain in the right hip. Paracentesis of the hip-joint showed pus. Cultures negative. A blood culture made at this time was negative.

March 25. Patient's condition has gradually improved, temperature normal, pain in right hip is lessening.

March 31. Temperature still normal, hip much improved.

April 3. At the time of this writing the patient's temperature has been normal for several weeks. Knee and hip in good condition, right eye much improved, patient apparently on road to recovery.

Diagnosis: Cerebrospinal meningitis and meningococcic septicaemia.

CASE III.—A. C. W., private, 313th Infantry, entered the hospital on January 26, 1918, complaining of indefinite pains in back and headache. On January 25, following a boxing match, he was taken with chills, fever and sweats. This was followed by headache, pains

in the back and bleeding from the nose, and the patient was admitted to the Base Hospital on January 26, apparently not very ill. There was no rigidity of the neck, only slight headache; no Kernig; no increase in reflexes. The eyes showed purulent conjunctivitis. The throat was congested; chest examinations negative. Over the whole body there was found a reddish, papular hemorrhagic eruption with marked itching. No skin parasites were found. The patient was quite dull and answered questions slowly. This dulness increased and shortly after admission the patient showed definite symptoms of meningitis. Spinal puncture was done immediately and the fluid was under marked pressure, purulent, and contained many meningococci. Intensive intraspinal and intravenous treatment were given. On February 4 the temperature was normal, headache and stiffness of the neck had disappeared and spinal fluid was clear; cultures were sterile. The patient was apparently convalescing rapidly.

On February 18, following an indiscretion in diet, the patient was taken with nausea, vomiting and headache and pains in the abdomen. Over the body were found a few petechial hemorrhages. A relapse was suspected and a spinal puncture was done immediately. The fluid was under marked pressure, purulent, and contained many meningococci. The patient's condition was very grave for several days, but he responded to treatment slowly, and within a week he was well on the road to recovery. Convalescence was uneventful and the patient was discharged cured.

Diagnosis: Cerebrospinal meningitis, with relapse.

CASE IV.—Lieutenant L. B., D. C., 154th Depot Brigade, entered the hospital January 12, 1918, complaining of general malaise and headache. His past history was negative, except for a marked predisposition to tonsillitis and "grippal" infection. On January 1 the patient had quite a severe attack of tonsillitis, with chills, fever and sweats. The condition grew progressively worse and January 10 he felt quite sick. He had a severe sore throat, slight frontal headache and general malaise. On January 11 he awoke with a violent throbbing frontal headache and marked pains over both eyes. January 12 and 13 the headache and pains above the eyes persisted; he felt chilly, feverish and stiff. He was then sent to the Base Hospital for treatment.

On admission the patient was quite rigid; Kernig and Brudzinski signs positive; neck quite stiff; reflexes markedly exaggerated and complaining of a terrible headache. Physical examination was negative except for peculiar pinkish spots over the chest, back and abdomen. They resembled hemorrhages into the skin. Tentative diagnosis of meningitis was made and a spinal puncture was done immediately. The fluid was under marked pressure and contained innumerable cells with a large percentage of polynuclears. A few meningococci were found in the smear. The patient was given stren-

uous intravenous and intraspinal treatment, and after the fourth day the symptoms subsided, the fluid became clear, the temperature dropped to normal and the patient was apparently convalescent.

January 29, eight days after the last spinal puncture, the patient was taken with a slight headache, stiffness of the neck and had a slight fever. Over the abdomen and chest were found a few pinkish hemorrhagic spots. Diagnosis of a relapse was made and spinal puncture was done immediately, with removal of 45 c.c. of cloudy fluid under marked pressure. The patient was again given intravenous and intraspinal treatment, and after seven days the symptoms subsided; fluid became clear, contained but few cells and was negative to culture. The patient was apparently convalescent. No punctures were done from February 6 until February 12.

February 12. The patient had a rise in temperature to 104° , slow pulse and a petechial, hemorrhagic eruption over the body and a marked headache. Spinal puncture revealed cloudy fluid under marked pressure, containing many meningococci. For the third time the patient was given intraspinal and intravenous treatment; the symptoms slowly subsided and on the fourth day he was apparently on the road to recovery. Due to the extreme number of relapses it was decided to give the patient occasional doses of serum, so punctures were done on February 19, 22 and 25, and serum was given intraspinaly.

February 28. Temperature was normal and the patient's condition is excellent except for a slight hypostatic congestion at the base of the left lung.

March 1. The patient had a sudden rise in temperature, headache and a few suspicious spots over the abdomen. Relapse was suspected and a puncture was done immediately. The spinal fluid was under marked pressure and very cloudy. On account of the extreme reaction which the patient exhibited to intravenous serum it was deemed advisable to discontinue the same and give simply three doses of intraspinal serum on consecutive days. The fluid became clear, temperature dropped to normal and the patient's condition became much improved.

March 11. From March 11 to March 16 there were chills, fever and sweats on every third day; leukocytes, 23,800; no malarial parasites found. Repeated blood cultures were sterile. Physical examination was negative except for occasional tender spots, which arose at various places during the paroxysms. These spots showed definite evidence of acute inflammation and were usually seen along the course of bloodvessels. Special examination of ear, eye, nose and throat and heart and lungs failed to reveal the cause of the paroxysms.

March 20. Chills, fever and sweats occur daily, especially in the afternoon. White blood count, 13,400; no malarial parasites found;

blood culture sterile. Nutrition and general condition of the patient is excellent.

March 28. The patient had a chill, fever and sweat, closely followed by marked headache and stiffness of the neck. Over the body were found a few petechial hemorrhages. This was exactly fifteen days after the last spinal puncture. Relapse was suspected and puncture done immediately. The fluid was very cloudy under marked pressure and contained 98 per cent. of polynuclear leukocytes. No organisms found. Temperature, 104°. The patient was given two doses of intraspinal serum and the temperature immediately fell to normal; fluid became clear and symptoms rapidly subsided. The temperature has been normal for one month.

Paroxysms of chills, fevers and sweats have disappeared. Spinal fluid is negative and the patient is apparently on the road to recovery.

It is well to note that at no time has the patient had a positive blood culture, also that each relapse was associated with a definite petechial rash and that the spinal fluid during all the relapses but two showed meningococci on culture, after cultures had been repeatedly negative during the quiescent stage.

Diagnosis: cerebrospinal meningitis, with relapses.

This case is notable for the number of relapses (five) and the fact that these relapses were apparently reinfections. As an attack subsided the organisms diminished from the spinal fluid, later the fluid becoming clear. During convalescent periods organisms could not be discovered in centrifugalized specimens of the fluid nor by culture. Also, it is to be noted that blood cultures taken at the onset of these relapses were in all instances sterile, although every precaution was exercised to protect an organism of delicate growth.

SUMMARY. Two cases of cerebrospinal fever, with initial septemia, are reported, the meningococci being present in the blood before demonstrable in the cerebrospinal fluid.

Two cases of meningitis with relapse are reported, the relapse taking the character of reinfection.

REVIEWS

MEDICAL WAR MANUAL No. 5. Authorized by the Secretary of War and under the supervision of the Surgeon-General and the Council of National Defense.

LESSONS FROM THE ENEMY: HOW GERMANY CARES FOR HER WAR DISABLED. By JOHN R. McDILL, M.D., F.A.C.S., Major, Medical Reserve Corps, U. S. Army. Philadelphia and New York: Lea & Febiger, 1918.

IT is safe to say that none of the series of medical war manuals, of which this is No. 5, exceeds the present small volume in general interest. It has the unusual advantage of reflecting conditions in an enemy country as they have been encountered there during the protracted residence and activity of the author. The paucity of contributions relating to enemy activities, however, does not alone supply the interest of this manual, as the author has presented within its compass a complete bird's-eye of the German medicomilitary organization.

The text is divided into twelve chapters and is profusely illustrated. Many of the illustrations consist of diagrams and scale elevations which relate, respectively, to organization and to the mechanical make-up of sanitary trains, railway ambulances and the like. There are also illustrations of equipment, hospital barracks, etc., but perhaps the most important are those referring to reëducation of the disabled, which show, very graphically, individuals and groups undergoing educational training. There are also excellent cuts of the many artificial limbs and prostheses now developed to such a high plane of utility.

The book begins with a consideration of the German medicomilitary organization and proceeds through administrative methods and the subject of base hospitals to the medical and surgical aspects of war, including voluntary and Red Cross nursing. The author specifically states that it is not the function of this book to detail purely medical and surgical considerations, although greater emphasis on the outstanding features encountered in his own experience would have been of undoubted interest. The balance of the book is devoted to the question of reëducation of the disabled, to the orthopedic hospitals and to the broader aspects of social and national relief work.

One of the most interesting chapters is that on administrative

methods and another concerns base hospital supplies, under which a table is given of the medicines issued. The brevity of this list is striking. In commenting on the character of the medical work in the German army the author says: "In general the surgery in German war hospitals was not as good as one had a right to expect. . . . the available competent men have not yet been made use of in the most efficient way."

It is rather interesting to note that no military patient is ever forced to submit to an operation, and *a propos* of the broad field of medical relief the author remarks: "It is a national game in psychology that all classes now are playing under the instructions of the medical faculty."

The book is open to a number of minor criticisms, beginning with the language, which is sometimes loosely constructed and often characterized by unnecessarily long sentences. The opening paragraph of the text illustrates this careless and ambiguous structure.

Space will not permit of enumerating the various side lights on conditions in Germany which a perusal affords, but it can be said, in summary, that this small work constitutes an interesting complement to the voluminous medicomilitary and rehabilitation literature compiled hitherto chiefly from the Allied stand-point.

R. P.

MEDICAL SERVICE AT THE FRONT. By LIEUT.-COL. JOHN MCCOMBE, C. A. M. C., and CAPT. A. F. MENZIES, M. C., C. A. M. C. Philadelphia and New York: Lea & Febiger, 1918.

THE authors of this little book state that it was begun at the suggestion of friends who desired to be told "something" about medical service at the front, and their effort reveals not only "something" but many things of interest in this connection. The text is preceded by a short foreword by Surgeon-General J. W. Fotheringham, D.G.M.S., Canada, before the war associate professor of medicine at the University of Toronto.

The book has the merit of great brevity, and described, with the aid of diagrammatic maps, the actual topographical disposition of men and things during advanced medical service. It is entirely free from unnecessary military technicalities and would seem to give, better than do most brochures of the kind, such a bird's-eye view as one might obtain could he hover in midair over the scenes of medical relief at the front.

Although compiled and written from the British stand-point the principles discussed are not detailed sufficiently to be confusing to students of our own methods; and it is to be recalled, furthermore, that many medical officers of our own army have long since seen service in the armies of at least one of our allies.

The language is for the most part clear and carefully chosen, the illustrations are excellent for the purpose intended and the book can be heartily recommended for those who desire information in this field.

R. P.

MEDICAL WAR MANUAL No. 6.

LABORATORY METHODS OF THE UNITED STATES ARMY. Compiled by the Division of Infectious Diseases and Laboratories, Office of the Surgeon-General, War Department, Washington, D. C. Pp. 256; 5 illustrations. Philadelphia: Lea & Febiger, 1918.

THIS little volume is in effect a condensation of standard laboratory methods, together with descriptions of some special method. The section on quantitative analytical methods was prepared by Dr. Donald D. Van Slyke.

Primarily the book is intended to give the experienced officer some standard of comparison. To those less experienced, it is a valuable guide. The technical procedures given are those which, in the opinion of the Surgeon-General, are the best available at the present time.

H. D.

PRACTICE OF PEDIATRICS. By CHARLES GILMORE KERLEY, M.D., Professor of Diseases of Children in the New York Polyclinic Medical School and Hospital, etc. Second edition. Pp. 913; 136 illustrations. Philadelphia and London: W. B. Saunders Company, 1918.

THE first edition of Dr. Kerley's *Practice of Pediatrics*, published in 1914, was well received by the medical profession. As a comprehensive and well-edited text-book on pediatrics it has won a place among the best text-books on this subject.

Since the first edition appeared the progress in pediatrics has been such that in publishing a new edition it was necessary to make many changes in the text.

The present edition presents twenty-five new articles as follows: stools; the ammoniacal diaper; amyotonia congenita; ptosis and dilatation of the stomach in older children; duodenal ulcer; mechanical agencies as cause of digestive disturbances; intestinal infantilism of Herter; Vincent's angina; septic sore throat (milk-borne); pollinosis, pollen disease, hay fever; hemophilia (bleeder's disease); dyspituitarism; dystrophy adiposogenitalis; orthostatic albuminuria; precocious menstruation and precocious maturity; congenital stridor; stammering; meningismus; psoriasis; acidosis; acetoneuria in children; pellagra; beriberi; blood transfusion and intramuscular injection; hypodermoclysis.

In addition to these new articles, sixteen of the chapters of the

original edition have been largely rewritten; while many lesser changes, including the removal of a great deal of old material have been made.

The article on stools is disappointing in that it is very general and sketchy. It is very necessary and highly desirable to present this subject to students and general practitioners in a clear, definite succinct manner.

Roentgen-ray studies of the stomachs of children has led to an increased interest in the study of digestive disturbances of long standing in children and to a broader knowledge of the anatomical conditions underlying and responsible for such derangements. Dr. Kerley's article on "Ptosis and Dilatation of the Stomach in Older Children," which is well illustrated with roentgenograms, shows the advances which have been made in the recent past in the study and treatment of these conditions.

What has just been said applies equally to an excellent article on "Mechanical Agencies in the Intestinal Tract as a Cause of Digestive Disturbances."

The discussions relative to acidosis, acetonuria, pellagra and beriberi present these subjects in accordance with our present-day conception of these conditions, which have recently received so much consideration and investigation on the part of scientific laboratory research and field workers. I. F. S.

PHYSICAL DIAGNOSIS. By W. D. ROSE, M.D., Lecturer on Physical Diagnosis and Associate Professor of Medicine in the Medical Department of the University of Arkansas. St. Louis: C. V. Mosby Company.

THERE may be some question as to the absolute need of such a book as this, inasmuch as it offers but little new to the subject-matter of physical diagnosis or its classification. It is, however, easy of reference and of possible value to students in the matter of definition and description of signs. Its explanation of the signs by the simple statement of facts, however, is apt to be misleading and does not permit a true interpretation of their value.

The subject-matter includes the physical examination of the respiratory organs, roentgenography and fluoroscopy and the diseases of the respiratory organs; the physical examination and diseases of the circulatory organs; general and special examination of the abdomen and its contained viscera; the examination of the head, neck and extremities and the examination of the nervous system. The description of the Bárány tests is especially well written, and a table showing the clinical facts upon which equilibrium tests are based is very complete.

An appendix gives a very full outline for a case history and physical examination. C. N. S.

NEUROSYPHILIS: MODERN SYSTEMATIC DIAGNOSIS AND TREATMENT PRESENTED IN ONE HUNDRED AND THIRTY-SEVEN CASE HISTORIES. By E. E. SOUTHARD, M.D., and H. C. SOLOMON, M.D. Pp. 496. Boston: W. M. Leonard.

THIS is a splendid and perhaps the best exposition of neurosyphilis so far published. While it has been written primarily for the general practitioner, nevertheless even the most accomplished neurologist can gain a great deal of information from its contents. The method of its presentation makes it particularly attractive to the student, for here the case method is used. The authors illustrate their points entirely from the citation of selected cases, which are well analyzed and logically arranged. From these case presentations classifications are built up, until finally every phase of the problem has been fully presented and discussed. It is possible by this method to adequately present the pathological data which the authors have had so much opportunity of studying. This of course makes the book so much more valuable.

In the treatment they emphasized the importance of the intensive method and state that this is the only method which gives results. They say further: "Some of the results give rise to greater optimism than has prevailed in asylum circles, especially in general paresis. We are confident that no one can now successfully make a differential diagnosis between the parietic and the diffuse non-parietic forms of neurosyphilis in many phases of either disease even with all laboratory refinements. If this be so it is improper not to give the full benefits of modern treatment to all cases in which the diagnosis remains doubtful between the parietic and the diffuse non-parietic forms of neurosyphilis. We ourselves advocate modern treatment, not only in the diffuse, but also in early parietic forms of neurosyphilis." A very valuable chapter was added on neurosyphilis and the war. They emphasize the very rapid development of syphilitic conditions under the strain and stress of war, this being one of the striking medical facts brought out by this great conflict.

T. H. W.

THE PRESCRIPTION, THERAPEUTICALLY, GRAMMATICALLY AND HISTORICALLY CONSIDERED. By OTTA A. WALL, Ph.G., M.D., Professor of Materia Medica in the St. Louis College of Pharmacy. Fourth and revised edition. Pp. 274. St. Louis: C. V. Mosby Company.

THIS book, for a long time a favorite among students, has been out of print for some years and its reappearance, thoroughly revised, will be a source of delight to students and to physicians desiring

to check up on careless habits of prescription writing. Of special value and interest is the section on the use of the metric system, and easy methods of acquiring the ability to write correct prescriptions of this kind are thoroughly explained.

Following the full discussion of weights and measures the author takes up the language of the prescription and very practically reviews the essentials of Latin grammar. In the matter of abbreviations he pointedly remarks that grammatical correctness or elegance are subordinate considerations. An error in a prescription which merely annoys a Latin scholar is absolutely insignificant when compared with an error which may lead to the dispensing of the wrong medicine.

The latter part of the book contains an exceedingly interesting history of the prescription which would be enjoyed by every practitioner.

The book is well written, with large type and large pages, and with the exception of some unnecessary repetitions of the subject matter is without criticism.

C. N. S.

BUILDING HUMAN INTELLIGENCE. By DR. ARNOLD LORAND.
Translation by PHILIPP FISCHER. Pp. 451. Philadelphia:
F. A. Davis Company.

THIS is a very interesting but rambling criticism of the common diseases of mankind, with constructive discussion of the method of building up the normal individual so that he can live and think better. The author for many years was a physician at the Baths Carlsbad, and therefore had wide experience with all sorts of internal conditions. He begins by discussing the influence of various factors on the faculty of thinking. This part is divided into nine chapters. In this he discusses the influence of metabolism, nourishment, climate, heredity, etc., making some very interesting and pertinent observations. In the second part he discusses the influence of sexual impulse and the sexual difference upon the intelligence. This part is very sane and well thought out. He next discusses the harmful influence upon the thinking ability and their treatment according to the newer principles. In this he discusses the causes of insanity and its prevention, the influence of alcohol, syphilis, thyroid gland and other diseases. One very interesting phase of his discussion of treatment is that he prescribes thyroid gland for practically every disease, even for the prevention of old age! He next takes up increase of thinking ability by hygienic and therapeutic means. This part is full of sane suggestions. He then discusses the power of thinking and rational thinking, their development particularly in practising the senses. He calls attention to the lack of use of the

senses in most individuals. He then takes up memory and its systematic development, rational mental work, rational development of intelligence in children and finally hygienic principles for a reform of school curriculum, particularly in high schools. As can be seen from these headings the author discusses many phases of the developmental problems of the human being, sometimes in a rambling, then again in a very intelligent, philosophical manner. The book is well worth reading and the reviewer read every bit of it with the greatest interest.

T. G. W.

DREAM PSYCHOLOGY. By MAURICE NICOLL. Pp. 194. Oxford Medical Publications. Henry Frowde and Hodder & Stoughton, Oxford University Press, Warwick Square, E. C., London.

THIS is a very interesting short analysis of dream psychology. As is well known in Freudian literature the so-called Jung school of Zurich is an outgrowth of the Freudian school at Vienna. In recent years Jung and his followers departed from the original principles as laid down by Freud, with the consequence that the latter has formally stated that Jung and his followers were no longer true psychoanalysts. The author takes Jung's view-point and gives his conception of dream psychology. These views are well known and need not be stated in this review. Interesting, however, is the fact that the author in his argument uses the shell-shock cases which he has had the opportunity of examining in England as examples of his psychology. He compares the mental state sometimes found in this condition with that found in childhood, and states that some of them are like infants and some are "even like infants unborn." They are alive but cannot see, hear or speak, a process according to him of "regression." This is interesting and represents one view-point of the psychoanalytic method of treatment even in such cases as shell-shock.

T. H. W.

STATE BOARD EXAMINATION QUESTIONS AND ANSWERS OF THE UNITED STATES AND CANADA. Reprinted from the *Medical Record*. Fifth edition. New York: William Wood & Co.

THE present is the fifth edition of this book, and the fact that over 13,800 books of the first edition have been distributed is an evidence that the work is appreciated. It contains the authentic questions and authoritative answers in full that have been asked by the Medical Licensing Boards of twenty-seven States and the Medical Council of Canada during the past year. It of course is

designed to be particularly useful to the recent graduate in familiarizing him with the nature of the examination to which he must submit before obtaining the right to practise medicine. Its use undoubtedly would be enhanced if the compilers had taken the trouble to arrange a suitable index. Notwithstanding this criticism, however, the fulness of the answers makes this edition of exceptional value to anyone desiring to review medical studies. C. N. S.

A CLINICAL MANUAL OF MENTAL DISEASES. By FRANCIS X. DERCUM, M.D. Second edition. Pp. 479. Philadelphia & London: W. B. Saunders Company.

THIS is the second edition, the first having appeared barely a year ago. There can be no better evidence of the popularity and need of this book. The second edition has not many changes. There have been some additions made in the treatment of dementia precox, and the author has added some of the recent advances in the pathology of paresis and has made some changes in the treatment. The chapter on psychological interpretation has been a little enlarged and rewritten in part, but no great change has been made; but the second edition is distinctly better than the first. As was stated in the first review it is a sane presentation of mental diseases from the clinical view-point. T. H. W.

THE MEDICAL RECORD VISITING LIST, OR PHYSICIAN'S DIARY FOR 1918. New York: William Wood & Co.

THIS handy little book is so well known that it needs no comment. Besides containing a weekly list it has appended useful tables of dosage and treatment of emergencies and an obstetrical calendar. C. N. S.

AMERICAN ILLUSTRATED MEDICAL DICTIONARY. Ninth edition, revised and enlarged. Edited by W. A. NEWMAN DORLAND, M.D. Pp. 1179; 331 illustrations. Containing over 2000 new terms. Philadelphia and London: W. B. Saunders Company.

THE ninth edition of this well-known and justly celebrated book has just appeared. It has been enlarged and brought up to date by the addition of more than 2000 words bearing upon the war and allied conditions. The mechanical work on the book is exceptionally well done, binding, printing, paper, etc., leaving nothing to be desired. C. B. S.

CHEMICAL PATHOLOGY. By H. G. WELLS, PH.D., M.D., Professor of Pathology in the University of Chicago and in Rush Medical School, Chicago; Director of the Otho S. A. Sprague Memorial Institute. Third edition. Pp. 707. Philadelphia: W. B. Saunders Company, 1918.

THIS valuable book is too well known to need any extensive comment. The entire work has been reprinted to embody the progress of the last three years in the chemical problems of disease. Many subjects have been rewritten, particularly gout, specificity of immunological reactions, anaphylaxis, icterus, acidosis, diabetes and uremia. New sections have been added on the Abderhalden reaction, specificity, chemical basis of growth, atrophy, and the pressor bases.

This edition contains much valuable information on the subject of carbohydrate metabolism resulting from work done in Dr. Woodyatt's own laboratory.

In spite of the war—and perhaps even because of the war—investigations in the chemical problems of disease have continued, so that the present work is a welcome record of newer research both at home and abroad.

H. D.

VITAL FUNCTION-TESTING METHODS. By WILFRED M. BARTON, M.D., Associate Professor of Medicine, Medical Department, Georgetown University; Attending Physician to Georgetown University Hospital. Second edition. Pp. 318. Boston: Richard G. Badger.

THIS book brings together in one volume the many functional tests bearing upon the diagnosis of diseases of the heart, liver, pancreas, kidneys and ductless glands, so that medical practitioners are in a position to make a more comprehensive diagnosis.

The fact that the work has gone into its second edition indicates readily the favor it has found among those of the medical profession who are interested in vital function testing.

The chapters on the heart and on the liver and kidney function have been enlarged. The latter include a description of the Van Slyke method of urea determination, test-meal investigations of kidney function, Ambard's coefficient and McLean's index of urea excretion, Creatinin and uric acid estimations in blood and a synopsis of Mosenthal and Lewis's scale of renal involvement.

References to the literature are given, and altogether the book should be of great value to the physician, instructor, clinician and pathologist alike.

H. D.

PROGRESS OF MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Ethyl Chloride as a General Anesthetic of Choice in Operations of Short Duration.—HAGLER and BOWEN (*Surg., Gynec. and Obst.*, 1918, xxvi, 352) say that when their American Unit assumed charge of the Graudenz (Germany) Reserve Hospital No. V, in July, 1916, they found that ethyl chloride had been employed frequently, though not extensively, for inducing general anesthesia. This practice they immediately ordered discontinued upon grounds of its extreme danger. They were induced by the assistants and Sisters to reconsider their action and to resume the practice in suitable instances, the number of which was abundant. They find in summarizing their observations that when clearly indicated, and when administered according to the described technic, ethyl chloride is preferable to local anesthesia, because the patient is spared all pain and because there is great conservation of time and energy. In the stress of active military service, simple and time-saving procedures are welcome aids. As compared with ether and chloroform, ethyl chloride has the advantages of being more rapidly effective, of producing a transient anesthesia from which recovery is immediate and of freedom from disagreeable after-effects. It is also simple of administration, and in an emergency may be given by persons altogether unskilled in the technic of anesthesia. When administered carefully and for short periods only it is apparently free from danger. It is not suitable for the reduction of fractures and dislocations on account of failure in producing thorough muscular relaxation. Its usefulness deserves wider recognition among members of the profession, and particularly among those at present engaged in the national service.

War Surgery of the Chest.—LOCKWOOD and NIXON (*British Med. Jour.*, February 2, 1918, p. 145) say that in no other branch of war surgery is the technic of the operation more exacting, although the

manipulations themselves do not require any exceptional dexterity. Chest cases are as urgent as abdominal cases and should be evacuated direct to the casualty clearing station as soon as they can stand the journey. The better the evacuation from the battlefield and from the advanced medical units the severer is the type of case that reaches the casualty clearing station. Thus deaths occur in the casualty clearing station that would otherwise take place farther forward. The percentage of severe chest wounds reaching the casualty clearing station is very much greater when the casualties are principally due to shelling and bombing, especially of the back areas, when the casualty clearing stations are the nearest medical units. Cases of traumatopnea should be closed (preferably by suture) at the advanced dressing station, or even, if possible, at the regimental aid post. Old chest cases should be given morphin early. Active resuscitation must be carried out at the casualty clearing station immediately upon admission. The majority of severe chest wounds require blood transfusion. The value of x-ray examination in chest surgery cannot be overestimated. The complete intrathoracic operation is a serious one and should not be lightly undertaken. Local anesthesia, combined with gas and oxygen (if required), should be employed in chest surgery. Speed and absolute asepsis are essential to success. The operation must begin with total excision of the wound and end with hermetical sealing of the thorax. No fluid must be allowed to collect in the pleural cavity after the operation. Resection and drainage should be a late resort, and are rarely necessary, never unless severe constitutional symptoms of infection are present. Non-operated cases should be treated precisely as postoperative cases. Men who have been exposed to asphyxiating gases bear chest wounds badly. At certain seasons bronchopneumonia is a complication greatly to be feared. In no class of surgery is team work so essential to success.

Treatment of Wounds of the Chest.—HUTCHINSON (*British Med. Jour.*, February 16, 1918, p. 196) says that all cases of wounds of the chest should be treated in special wards or special hospitals. Careful charts should be kept which record temperature, pulse and respirations four times a day. Early diagnosis of infection is important. Every case in which there is more than two finger-breadths of dulness should be aspirated. Cases of open pneumothorax should be closed as early as possible. Cases in which there is a large amount of clot in the chest should be opened, blood and clot evacuated and the chest closed. This should be done as early as possible. Cases in which the hemothorax is found to be infected should be opened, washed out and closed, some antiseptic being left in, preferably an emulsion of bipp in liquid paraffin. Postoperative aspirations must be done in all closed cases the first forty-eight hours after operation. No attempt should be made at the base in France to remove a foreign body from the lung.

The Guillotine Amputation.—MURRAY (*British Med. Jour.*, February 23, 1918, p. 230) says that it is unfortunate that so few surgeons working at the front have not had the opportunity of seeing the after-results of the guillotine method. It may be that the fear of gas gangrene is the important factor which has caused this plan to be adopted so generally.

A guillotine amputation invariably necessitates reamputation, but apart from this the great disadvantage is that by the time the patient arrives in England the skin has retracted so much that a large granulating and suppurating stump is exposed. The dressings are often extremely painful and the subsequent loss of bone, even after prolonged extension to draw the skin down, is sometimes very great. If surgeons in France decide that after all it must be a guillotine amputation it is hoped they will so modify it as to leave much more skin and so dispense with many subsequent troubles and save the ultimate length of the patient's limb.

Pulse Rate and Blood-pressure Observations as an Aid in the Treatment of Head Traumas.—SIEBER (*Ann. Surg.*, 1918, lxvii, 51) says that a rapid encroachment upon the intracranial space by any foreign body produces anemia of the brain and medulla and is associated with a physiological response represented by an increase in the general arterial pressure and decrease in pulse rate. The associated intracranial pressure complications are the dangerous factors in fractures of the skull. When the degree of intracranial pressure equals or exceeds the arterial pressure death results. Frequent blood-pressure and pulse-rate observations not only determine the degree of intracranial pressure but may be utilized as indications for or against the advisability of relieving the pressure. Intracranial pressure should be relieved before the advanced stage of medullary compression and edema is produced. The subtemporal decompression is the advisable method for relief of intracranial pressure. By frequent blood-pressure and pulse observations fractures of the skull may be divided into three groups: (1) Those cases which at no time show any evidence of intracranial pressure; (2) cases presenting definite signs of increase of intracranial pressure; (3) cases presenting signs of advanced medullary compression or in which there is evidence of severe laceration or contusion of the brain.

A Study of Ante-operative and Post-operative Blood Counts in Non-infective Surgical Conditions.—MELENEY (*Ann. Surg.*, 1918, lxvii, 129) says that in surgical cases undergoing operation without infection the white cells increase in number, and about six hours after operation have more than doubled. The response is due almost entirely to the outpouring of polymorphonuclear cells. There is a trivial rise in red cells after operation, but in the subsequent ten days this is followed by a progressive anemia, with an average loss of about 500,000 cells per cubic millimeter. The white cell count may be expected to fall rapidly in clean cases and reach normal on the fourth day. In infected or contaminated cases it will fall much more slowly. Infection and contamination have nothing to do with the initial rise, but on the second or third day after operation they will tend to keep the count high. Other things being equal the count will be higher in those cases in which there are severe trauma to the tissues, many sutures and ligatures used, considerable loss of blood and long anesthesia, especially with ether. Normal individuals will produce a higher leukocytosis than abnormal types.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND
SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Rate of Absorption and Excretion of the Iodides of Strontium, Sodium and Potassium.—KRAHULIK and PILCHER (*Arch. Int. Med.*, 1918, xxi, 176) conclude from their experiments on human subjects that there is practically no difference in the rate of excretion of the iodides of strontium, sodium and potassium. After ingestion of the corresponding doses of iodide the rate of excretion rapidly increases, reaching its maximum at about the sixth hour, and then decreases rapidly, so that during the third day but 10 to 20 mg. are excreted. A somewhat greater quantity of strontium iodide than of sodium is excreted during the twenty-four-, forty-eight- and seventy-two-hour periods. The difference is slight and probably of no clinical significance. There seems to be no definite ratio between the excretion of iodide and the volume of the urine, in some instances a large volume of urine is associated with a greater excretion of iodide, in others the reverse is the case. About an hour after taking iodide two of the subjects complained of soreness of the pharynx, which persisted for several hours. There was no apparent difference from the different iodides in the time of onset, intensity and duration of the symptoms. A third subject noted an acne eruption of the same degree from the strontium and sodium salts. The authors conclude that the prevalent idea that strontium iodide is more slowly absorbed than the potassium and sodium salt is erroneous. In fact the rate of absorption of strontium iodide is at least as rapid as the rate of absorption of the other salts examined, and both the rate and total excretion seem to be slightly greater with strontium iodide, although the difference is so slight that it is of no clinical significance.

The Value of the Atropin Test in the Diagnosis of Typhoid Fever.—MASON (*Arch. Int. Med.*, 1918, xxi, 1) reports the results of 306 atropin tests performed on 63 patients suffering from typhoid or paratyphoid B infections and on 46 non-typhoid patients. The technic employed by Mason was substantially that introduced by Marris. The average mean pulse rate was obtained by counting the pulse for ten consecutive minutes while the patient rested quietly in bed. The atropin (gr. $\frac{1}{30}$ or gr. $\frac{1}{33}$) was injected subcutaneously, and after twenty minutes the pulse rate was again taken and counted every minute until the acceleration had reached and definitely passed its maximum. The difference between the maximum acceleration and the average mean pulse rate is taken as the "release." Marris found that in most normal persons the increase in pulse rate (the release) was from twenty to forty beats per minute, and that a release of ten beats or less per minute was suggestive of enteric infection. Mason carried out 256 tests on 58 cases of typhoid fever (diagnosis confirmed by blood culture or positive

Widal reaction in 56) and 5 cases of paratyphoid B infection. Eleven of these 63 cases failed to give a positive atropin reaction, that is, a release of ten or less. This high percentage may be accounted for by the fact that 6 of the 11 patients received only one test, and that 3 were extremely restless and toxic. On the average the test appeared on the eleventh day of the disease and disappeared on the thirty-first day. In 12 of 35 cases the atropin test appeared before the Widal, and in 4 it was positive before either the Widal or the blood culture. Of 46 non-typhoid patients 3 gave positive reactions. These patients suffered from acute bronchitis, tuberculous meningitis and diabetes mellitus respectively. The average release of all other non-typhoid cases was 23.9 (extremes 11 to 54). The maximum acceleration appeared 33.5 minutes after injection. From his results, Mason concludes that in the diagnosis of enteric infections the atropin test is of great value.

Common Colds as a Possible Source of Contagion for Lobar Pneumonia.—VALENTINE (*Jour. Exp. Med.*, 1918, xxvii, 27) recovered pneumococci from 43 out of 65 cases of common colds. The incidence of type or group was as follows: Group I, 2 cases; Group II, 2 cases; Group III, 4 cases; Group IV, 35 cases. The cases from which Group II was isolated and one of the Group III cases had been in contact with pneumonia, and it was not possible to decide whether they were merely contact carriers or whether the cold was an actual infection by pneumococci due to contact with the pneumonia cases. In two instances, with no known contact with cases of pneumonia, pneumococcus Type I was found to be the predominating organism, which strongly suggests that it was the etiological agent in these colds. If this is so, common colds of this type must be looked upon as a possible source of contagion in the development of lobar pneumonia due to Type I pneumococcus.

Further Observations on the Clinical Actions of Veratrum.—This report (*Jour. Pharmacol.*, 1918, xi, 89) is a continuation of the previous work of COLLINS and HANZLIK on the clinical action of veratrum album, and comprises 36 observations on 27 different patients suffering from nephritis, typhoid, tuberculosis, eclampsia, etc., and various circulatory disturbances and on two normal persons. The preparation employed was the 10 per cent. tincture of veratrum album administered with one or two tumblers of water to allay gastric irritation. During the observations all patients were lying quietly in bed. The pulse rate was taken every fifteen minutes and blood-pressure was estimated (auscultatory method) every fifteen to thirty minutes. The following is a summary of their findings: Single therapeutic doses of from 15 to 20 minims caused a slowing of the pulse and a fall in blood-pressure, and this occurred independently of such symptoms as nausea and vomiting. Large and repeated doses (25 to 75 minims) caused a fall in both systolic and diastolic blood-pressure and a diminution in the pulse rate roughly proportional to the dose. In the 11 cases of circulatory disorders the effect was most marked in hypertonus (6 cases); less marked, inconstant, or no effect at all in heart block (2 cases), paroxysmal tachycardia, myocarditis, with renal vascular disease, aortic insufficiency (1 case

each). There were no demonstrable effects on the electrocardiogram. The two normal individuals responded to the drug in the usual way. There was practically no effect on respiration from either large or small doses. Control experiments (five) with compound tincture of gentian (U. S. P.) administered under the same conditions as tincture of veratrum album to the same and other individuals, showed no noteworthy effect on the circulation. The effects of veratrum are due therefore to the drug *per se*. They conclude that all the desirable circulatory effects produced by tincture of veratrum album may be secured with doses ranging from 45 to 55 minims administered at the rate of about 10 to 15 minims every half to one hour. Large doses repeated at short intervals are apt to give rise to toxic symptoms, such as nausea, vomiting and some depression. These effects are generally absent with small doses given at longer intervals.

Experimental Studies of the Mode of Absorption of Mercury when Applied by Inunction.—SCHAMBERG and his collaborators (*Jour. Am. Med. Assn.*, 1918, lxx, 142) devised an ingenious experiment to settle the vexed question of the mode of absorption of mercury when applied by inunction. A box was divided into two compartments by means of a partition. In one part was placed Rabbit A (which was to receive the inunctions), with its head projecting into the outer air through an aperture in the end of the box. Rabbit B (the control) was placed in the other compartment with its head projecting through the partition into the compartment in which Rabbit A was confined. Rabbit B was thus constantly breathing an atmosphere heavily charged with mercury. From 0.5 to 1 gm. of mercury per kilogram (about fifteen times the amount used therapeutically) in the form of a 50 per cent. mercurial ointment or a 50 per cent. calomel ointment, was rubbed into the denuded skin of the back of Rabbit A. The inunctions were repeated two or three times in all within periods of from five to nine days. In every case Rabbit A died after a brief period and chemical examination showed considerable quantities of mercury in the kidneys and liver. These findings, taken in conjunction with the microscopic study of the organs, warrant the conclusion that the rabbits died of mercurial poisoning. The control rabbits remained in good condition. Those controls which had inhaled a metallic mercury atmosphere showed traces of mercury in kidneys, lungs, etc. (in one case a considerable amount), but there were no histological changes in the organs. When calomel ointment was used no mercury was found in the tissues of the control rabbits. The experiments were repeated five times, with similar results. These experiments demonstrate that the chief avenue of absorption of mercury, when applied by inunction, is the skin and that rabbits may be fatally poisoned with mercury even when no opportunity of absorption through the lungs exists. Metallic mercury in the form of the official mercurial ointment is more volatile and is much more apt to be absorbed through the lungs than calomel ointments of equal strength. The authors recommend the use of calomel ointment for inunctions on the ground that it is more cleanly than and at least as readily absorbed as the extremely dirty blue ointment.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Attempted Abortion in the Absence of Uterine Pregnancy.—STEIN (*Am. Jour. of Obstetrics*) reports several cases in which a patient was supposed to be pregnant and an attempt made to secure abortion. Various means were used: in one a stick of alum was inserted into the uterus, followed by chill, fever, infection, and death; in another, intra-uterine injections were given, followed by parametritis. In another case cited an attempt to push a blunt, irrigating tube into the uterus caused rupture in the deeper portion of the vagina. The wound was sufficiently extensive to require suture, after which the patient recovered. Catheters, douches, tubes, and other rod-like bodies have been repeatedly used for this purpose. Injections of bichloride of mercury have been employed, leading to fatal bichloride poisoning. Portions of catheters and tubes have been broken off and retained. It is impossible to secure an accurate account of these cases, but there are reported between 30 and 40. The laws of several continental countries punish attempted, unaccomplished abortion with imprisonment from some months to a year. In other communities the actual performance of abortion is considered the criminal element.

The Kangaroo Walk in the Management of Puerperal Retroversion.—BECK (*Am. Jour. of Obstetrics*) states that up to a year ago from 20 to 25 per cent. of hospital cases returned to the postpartum clinic with retroverted uteri. In the maternity wards the usual measures were taken to prevent this condition. At the end of the second week examination usually revealed no tendency toward retroversion, but one woman out of every four or five who returned to the clinic a month after discharge had a retroverted uterus. From this it was inferred that many cases became retroverted after going home. To obviate this what was called the kangaroo walk was instituted. This consisted of walking on the palms of the hands and on the feet, with the knees held as stiffly as possible; all constriction of the abdomen by corset or skirt bands was removed and high shoes could not be worn. Accordingly, these exercises were taken before the patient was dressed for the street. This was begun on the ninth day after delivery, and finally was increased until the patient walked five minutes in the morning and five minutes at night. Examination during the later part of the second week of the puerperal period showed that with the patient in this position the fundus falls forward and out of the pelvis, resting on the abdominal wall a little above the symphysis. The cervix is carried posteriorly and moves slightly with each step. There is a distinct lateral rocking of the pelvis, and, as the result of this, involution is stimulated and the tendency toward retroversion markedly lessened. Of 82 cases less than 10 per cent. had

retroverted uteri. Three of these 8 cases stated that they had carried out the exercises for sixteen days or more after leaving the hospital; 2 continued for six days, and the remaining 3 stopped in less than six days after their discharge. The remainder of the 82 had carried out the treatment faithfully, and with the best possible results. Involution proceeds far better with this treatment than in ordinary cases.

Phenol Excretin in the Urine of the Newborn.—MOORE (*American Journal Diseases of Children*) in a series of 15 infants found that the phenol excretion in proportion to the body weight is less in breast-fed than in artificially fed infants. There is, in infants and in adults, a relation between the total phenol excretion and the amount of proteid taken into the body as measured by the total nitrogen excreted in the urine. Recent investigations show that phenol is quantitatively present in the urine of every newborn infant. The average of 19 cases was 11.2 mg. for the first two days of life. As this is a period of starvation the phenol must originate in part through endogenous metabolism.

Postpartum Hemorrhage.—RICE contributes a paper upon this subject based upon his experience at the Manhattan Maternity of New York City. In 13,000 deliveries there was postpartum hemorrhage in 222 cases, 1 in 58. Among these there were 4 deaths, laceration of the cervix caused hemorrhage in 8 cases not associated with placenta previa. In 3 of these it was necessary to apply suture; the others were treated by hot vaginal douches. In 2 cases of rupture of the uterus the extent of the laceration into the broad ligament was not recognized and packing was used instead of suture. In cases where hemorrhage is due to laceration of the cervix, this fact should be ascertained as soon as possible, and sutures promptly inserted. If the tear has invaded the broad ligament, packing will not control it. In 1 case of laceration of the perineum and 1 of laceration involving the veins of the vestibule, there was profuse hemorrhage until sutures were applied. Prolonged labor, deep anesthesia with chloroform, and shock in operation predispose to hemorrhage. Local causes are substances retained within the uterus, as placenta, membranes or clots. Adherent placenta due to chronic endometritis may cause postpartum hemorrhage, and in these cases the placenta is partly adherent, leaving open sinuses in an operation of the uterine wall. A fragment of retained placenta, no matter how small, may cause hemorrhage even late in the puerperal period, and in one case hemorrhage was so severe as to be nearly fatal on the seventh day. Retained membranes are less important than retained placenta, and the chorion is much more apt to give trouble than the amnion or decidua. When the placenta is delivered too soon the membranes become separated and retained. "Hour-glass contraction" of the uterus is usually caused by improper efforts to deliver the placenta, and rarely occurs under good management. Twins, hydramnios and fibroids occasionally cause postpartum hemorrhage. The most severe form of postpartum bleeding occurs in placenta previa. In 57 out of 75 cases postpartum hemorrhage was present. While in many patients the blood comes from the placental site, in the majority of cases the cervix is torn sufficiently to cause bleeding. As the tear is through a portion of the uterus where there

is no contractive tissue, uterine contractions alone are not sufficient to stop bleeding, and packing is necessary. In 57 cases of postpartum hemorrhage due to placenta previa, there were 2 deaths. One of these was a case of central placenta previa with a cervix dilated only sufficiently to admit two fingers. A bag was used to dilate the cervix, one hour and fifteen minutes being employed for this purpose, and a stillborn child was then delivered by version and extraction. The question naturally arises, would not this patient's chance have been better if Cesarean section had been promptly done? The second case had a severe hemorrhage at her home, controlled by vaginal packing. The removal of this pack was followed by repeated hemorrhage and the patient was treated by version and extraction; death followed from hemorrhage and shock. In 9 cases where packing was used to control the hemorrhage from placenta previa, 5 had temperature during the puerperal period. In outdoor service cases are sometimes delivered before the arrival of the doctor or student, and in 1006 such cases there was excessive hemorrhage in 3 only. A case was described in which the patient had a long second stage in labor terminating in spontaneous delivery. The uterus did not well contract and hot douches, ergot and pituitrin were given, but at the end of two hours the patient's condition not being satisfactory, the uterus was packed with gauze. This was unsuccessful and the patient died from shock.

Subcutaneous Symphyseotomy.—BURKHARDT (*Correspondenz-Blatt f. Schweizer Aerzte*) has developed the technic of subcutaneous symphysiotomy, and finds Frank's subcutaneous method easy to apply and requiring no special instruments. Incision is made in the lower part of the symphysis and in the suspensory ligament of the clitoris, which allows the latter and the urethra to sag loosely, leaving an open space between the edge of the symphysis and clitoris region. There is no special danger of injury to the soft parts even in young nulliparæ. The incision of the skin is not longer than the width of the blade of a scalpel, and can be sutured securely. The cutting from below upward is of advantage and greatly lessens the risk of cutting important organs and tissues. The writer found the symphysis from 36 to 51 mm. high and from 18 to 26 mm. thick in 14 female cadavers.

The Treatment of Eclampsia by Vaginal and Abdominal Section.—BRODHEAD (*American Journal of Obstetrics*), believes that veratrum viride is valuable in cases of eclampsia where the heart is not especially weak. Elimination should be vigorously pushed. Delivery as soon as possible he considers imperative provided the mother is spared extensive lacerations. His choice of a method would depend upon the degree of softening and dilatation in the cervix, the size of the pelvis, the parity and environment of the patient, and the surgical skill and experience of the obstetrician. Where the cervix is not softened and easily dilatable, he would use the de Ribes bag. Where eclampsia appears before labor has begun, induction of labor by the bougie or the rectal tube and the bag is indicated. When the patient is in hospital under the care of an expert obstetrician, vaginal hysterotomy from the fifth to eighth months of pregnancy in cases where the cervix is

long and rigid, will give the best results. Abdominal section has frequently been performed. At the Harlem Hospital 34 cases of eclampsia are reported with twelve deaths, a mortality of 35 per cent. In 14 cases treated by vaginal hysterotomy the maternal mortality was 28.5 per cent. The writer endeavored to obtain records by corresponding with those who had performed abdominal Cesarean section for eclampsia and he secured reports of 174 published and unpublished cases. The maternal mortality was 16.1 per cent., and a number of cases died of conditions which could not be properly ascribed to toxemia. The fetal mortality was 18.8 per cent. The conclusions which the writer reaches are that conservative treatment in the majority of cases in eclampsia gives good results, but where labor fails to develop and there is unusual resistance in the birth canal, that delivery by vaginal or abdominal section at the earliest possible moment is indicated.

SPALDING (*Am. Journal of Obstetrics*) has seen good results in private practice in preventing eclampsia by careful hygiene. When this threatens to be unsuccessful, induction of labor has given satisfactory results. In 20 cases treated for eclampsia at his clinic or seen in consultation, 8 were at home amidst poor surroundings and with meagre assistance, with a maternal mortality of 50 per cent. and a fetal mortality of 37.5 per cent.; of 12 patients treated in hospital, the mortality rate was 25 per cent.

Postpartum Eclampsia with Death and Autopsy.—KEILTY and TAYLOR (*Am. Journal of Obstetrics*) report the case of a well-developed young woman who was delivered of twins and afterward had violent eclamptic convulsions dying sixty-five hours after delivery.

Separation of the Pubic Symphysis and Forceps Delivery.—ALLEN (*Am. Journal of Obstetrics*) reports the case of a primipara, aged twenty-four years, who had been delivered by forceps of a living child thirty-six hours before she was seen by the writer. The soft parts were greatly lacerated and there was loss of control of the bladder. There was a separation of the pubic joint of over three inches. This was easily reduced but it was difficult to maintain the bones in good position, so the application of a Lane plate was carried out. The patient did not have good nursing and this operation was a failure, the separation remaining what it had been before, and a small fistulous opening extending to the loose end of the plate. The patient was transferred to hospital where two one-half-inch incisions were made over the iliac crests at the upper anterior iliac spines, and two ordinary wire nails were driven into the iliac crests and left protruding above the skin about one-half inch. Sterile iron wire was wound tightly around the nails from one side to the other across the abdomen, and a tightly fitting plaster cast was put about the pelvic bones. While this was setting, the patient was held up in a sling and afterward put in a trough-shaped bed. In eight weeks her recovery was complete and two years after operation she remains in good health.

A Case of Cerebral Tumor Complicating Pregnancy.—MACFARLANE (*Am. Journal of Obstetrics*) reports the case of a pregnant woman who had been trephined for cerebral tumor. She became imbecile and

had convulsions for several days preceding labor. The birth of the child occurred in one of these convulsions, the child was living and the placenta expelled in twenty minutes. The patient died two days after delivery and no autopsy could be obtained. The obstetric interest of the case lay in the fact that labor was comparatively short and easy in view of the cerebral condition.

Eclampsia without Convulsions.—CHATILLON (*Correspondenz-Blatt f. Schweizer Aerzte*) reports the case of a primipara, aged forty years, who was apparently healthy during pregnancy and had a spontaneous delivery. Almost immediately after the placenta had been expelled the patient had rapid and weak pulse, grew pallid with cold extremities, and within an hour and a half died. There was no unconsciousness and no convulsions, but autopsy showed hemorrhage into the gall-bladder with extensive bleeding in the liver and minute hemorrhages in many other portions of the body. The right ureter was dilated and so was the pelvis of the right kidney; the child was in a condition of pallid asphyxia at birth and could not be revived. These cases are comparatively rare and are described by some as eclampsia without convulsions, and by others as acute fulminant toxemia. They are invariably fatal and no form of treatment at present known has the slightest effect upon them.

The Management of the Third Stage of Labor.—GIBSON (*Surgery, Gynecology and Obstetrics*) criticises the usage, which is common, of holding and massaging the uterus immediately after the delivery of the placenta. He calls attention to a physiological period of uterine inertia which immediately follows the complete emptying of the uterus, and lasts from five to fifteen minutes. He believes that the use of the Credé method before the placenta has completely separated is a very serious blunder and should be strongly discouraged. In studying the third stage of labor he finds that the placenta separates rapidly when massage is not practised, that bleeding is less, and that the fetal surface of the placenta presents much more frequently in these cases than when massage is practised. He draws attention to the fact that during separation the uterine sinuses are closing by thrombosis at the placental site and that massage must disturb essentially this important process. He follows Tarnier's advice that after labor one should watch constantly, but interfere as little as possible.

The Action of Pituitrin on the Human Uterus.—CHARTERIS (*Glasgow Medical Journal*) tested the uterus of pituitary solution to observe the action of the drug on the tissues. On investigating the non-pregnant tissue material obtained after early abortion, and the uterus removed by Cesarean section at full term, there seemed to be no difference between the action of the pituitrin on the pregnant and non-pregnant uterus. Both contracted, and a rapid response followed the use of the substance. Uterine contractions are more numerous; the individual contraction occupies less time and is followed by a more prompt relaxation, but the general tone of the uterus was markedly increased. The action of pituitrin is very prompt. Within a minute a stimulation which lasted from fifteen to thirty minutes was secured.

A second dose renews the original effect or intensifies the action already produced. In comparison with other substances, none were so efficient. Ergot was unreliable, and only the most recent preparations were active. So far as these experiments went, pituitrin was the most efficient and rapid agent for securing uterine contractions.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Iodide Solutions in Roentgenography.—The use of thorium solutions as opaque media in pyelography has practically superseded the old colloidal silver solutions on account of the greater safety, but one objectionable feature against thorium is the amount of care necessary in making a satisfactory solution. A more common and inexpensive substance whose aqueous solution is neutral would be preferable. For this purpose CAMERON (*Jour. Am. Med. Assn.*, lxx, 754) suggests a 50 per cent. solution of potassium iodide, which is almost completely opaque to the roentgen rays. The solution is perfectly clear and is strongly saline in taste, but not irritating to the tongue. It has a low viscosity, can be readily sterilized by boiling and is miscible with urine and blood without causing any precipitation or coagulation. The important question as to the possibility of these solutions causing toxic effects or local irritation is being thoroughly investigated. Though from the nature of these substances no such effects are anticipated, it cannot be stated now that they are entirely innocuous. However, Cameron has used solutions of high concentration in the kidney pelvis of the lower animals, and has used a 15 per cent. solution in the human bladder, and no undesirable effects of any nature have been encountered. Excellent roentgenograms were obtained in all instances.

Ureteral Stricture.—Ureteral stricture, or narrowing of the ureteral lumen, due to intrinsic inflammatory changes in the ureteral wall is a disease far more common and of vastly greater importance than the literature or our previous experience has led us to believe, states HUNNER (*Bull. Johns Hopkins Hospital*, 1918, xxix, 1), in presenting a paper based upon an experience with over 150 cases of this condition. According to him the majority of ureteral strictures, excluding those of tuberculous origin, should be classified as simple chronic stricture, and they have their origin in an infection carried to the walls of the ureter from some distant focus, such as diseased tonsils, sinuses, teeth or in the gastro-intestinal tract. This conception of stricture postulates that in the majority of cases ureteral infiltration is primary, and that the other urinary tract lesions so often associated with stricture, such as stone in the ureter, hydronephrosis, pyelitis and pyonephrosis, are secondary.

In substantiation of this assumption, Hunner has had a few cases which have persistently showed no material improvement in symptoms until after the removal of infected tonsils or teeth, and another list of patients who have been dismissed as well after dilatation of the strictures or after getting rid of the pyelitis by dilatation of the stricture and lavage, and who have returned with their old symptoms after a fresh tonsillitis attack or after undergoing dental work. Regarding the symptoms that are presented by these cases of ureteral stricture, it may be stated that pain is the most common, and only in rare cases is it absent. To attempt to draw a pain chart of this affection one would need a diagram of the human frame extending from the diaphragm to the ankles. The most deeply shaded portion of this chart would center in the local area of ureteral inflammation, or in other words, in the broad ligament region deep in the pelvis. From this center of inflammatory discomfort in the pelvis the pain may radiate in any direction, upward toward the kidney, laterally into the hips or groin region, posteriorly, simulating a sacro-iliac joint condition or a sciatica, and downward into the thigh and leg either posteriorly or anteriorly. Next in frequency to the local ureteral pain is pain in the kidney region. This is probably at times a referred pain from the inflammatory area in the ureter, but it is usually due to overdistention of the pelvis of the kidney. The urine may be quite negative on repeated careful centrifuging and microscopic search. Chills and fever are common in cases with urinary infection. A patient with infection may go for weeks or months without chills or appreciable fever and, indeed, may be in apparently perfect health, or may suffer only from malaise and general depression. The stricture is located in the broad ligament region or within 6 cm. of the bladder in by far the greater number of cases. The next most frequent location is at the bifurcation of the internal iliac vessels or about 8 to 10 cm. above the bladder which is from 3 to 5 cm. below the pelvic brim. In both of these regions there are groups of lymphatic glands and at operation these are sometimes found enlarged. The inflammatory area itself varies from a slight annular thickening in the ureteral wall to a condition of diffuse cartilage-like thickening which may occupy several centimeters of the ureter and form a mass a centimeter in diameter, while multiple annular strictures are not uncommon. One of the most interesting side-lights on ureteral disease furnished by this study has been the revelation of the probable cause of most ureteral stones. In operating for a ureteral stone and finding it encased in dense infiltration tissue we have heretofore considered the inflammatory area as due to the irritation of the stone. At present, however, there is abundant evidence to indicate that the stone results from urinary salts being deposited on the inflamed surface of the stricture area. The diagnosis of ureteral stricture depends upon the history, urinary examination, palpation of the abdomen, with special reference to the kidney, and ureter regions, palpation of the ureters through the vagina or rectum, cystoscopy, catheterization of the ureters by specially prepared catheters, and roentgenography. Cystoscopy is usually quite negative, but in the occasional case in which the stricture is near the bladder wall there may be redness and edema about the ureteral orifice, suggesting the picture seen with a low ureteral stone. One of the most suggestive

points in cystoscopy is the finding of a urethral stricture when preparing the urethra for the cystoscope. Although stricture of the female urethra is common after a gonorrhoeal infection, Hunner has learned by experience to give its presence considerable weight in the diagnosis of a suspected ureteral stricture. The crucial test, however, in diagnosing ureteral stricture is made with the wax-bulbed catheter. The chief end sought in the treatment of this condition is the relief of symptoms, and in the infection cases a urine freed from infection. In all cases suitable for dilatation such a thorough opening of the stricture area should be made that there will be no recurrence. There are very few cases in which the symptoms cannot be ameliorated, and fortunately, in the majority of cases, the patients can be relieved to a large extent if not entirely. There are very few cases of pyelitis in which the infection cannot be controlled, but Hunner believes that time will demonstrate that in many cases it will be impossible to get a permanent dilatation of the stricture and complete relief of symptoms until the original focus of infection has been eradicated. When all the methods of vesical approach fail we have to consider operative measures. No form of operation should be undertaken until as complete investigation as possible has been made of both sides. Stricture of the ureter being bilateral in 30 per cent. of the cases, we cannot afford to take anything for granted in dealing with a case in which symptoms may be confined to one side.

Renal Tuberculosis.—BUGBEE (*Surg., Gynec. and Obst.*, 1918, xxvi, 479) states that the present status of renal tuberculosis may be summarized by stating that it may be a primary lesion, and it arises from a filtration of tubercle bacilli from the blood stream into the parenchyma or tubules of the kidney, where changes similar to those found in tuberculous foci in other parts of the body take place. An effort is always made to wall off the process, but the formation of antibodies is so slow and the immunity of the patient, which may have always been absent or which may have been temporarily diminished, is so low that the lesion usually gets beyond control, and usually goes on to wide destruction of the kidney and extension to the other kidney, to other parts of the urinary tract and of the body. From the nature of the lesion, remissions are common and the symptoms of renal tuberculosis are misleading, often slight at the onset, giving no indication of the extent of the lesion. The diagnosis of this condition may be simple or, on the other hand, the most difficult of all urinary lesions, often requiring preliminary treatment to allay acute symptoms and repeated cystoscopic examinations over a long period of time. The treatment cannot be outlined from a study of the symptoms, but it is most important that the remission of symptoms, often for long periods of time, should not be accepted as a cure. The effort on the part of nature to inhibit the progress of the disease and to limit the lesion should be borne in mind, utilized and encouraged in every possible manner in inoperable cases as well as before and after operation. Occasionally the lesion may become arrested and walled-off but even when arrested, a kidney the site of poorly drained cavities is a menace to the system, therefore, nephrectomy for unilateral renal tuberculosis is the proper treatment.

OPHTHALMOLOGY

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,
DENVER, COLORADO,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,
PHILADELPHIA.

Insects as Possible Carriers of Poliomyelitis Infection.—C. T. BRUES (*Department of Health, New York City, Reprint Series, No. 60, July, 1917*) states that some new facts of interest and importance relating to the possible transmission of poliomyelitis by insects have resulted from his study of the epidemic of poliomyelitis in New York City during the summer of 1916, but these facts are not so definite or complete as had been hoped. They are also to some extent of apparently conflicting nature, and require at least one unproven assumption to combine them into any working hypothesis. They do not completely disprove the idea that the table-fly (*Stomoxys calcitrans*) is implicated, although the behavior of the epidemic does not favor this view. The author thinks that to discard the insect-borne hypothesis is to cast aside evidence derived from two sets of experiments, and he regards it unwise to do this at the present time of uncertainty. As suggested by Richardson, it is possible with one assumption to form a working hypothesis based upon rats and fleas which seem to fit the epidemiological observations in general features and in many details as well. The assumption that the rat can act as a reservoir for the poliomyelitis virus should be capable of experimental proof, and it would seem that such experiments should be attempted. This by no means precludes the association of some other insect or warm-blooded animal, or both. In fact, there is a continual appearance of circumstantial evidence that suggests a population other than the human one, acting as an undercurrent and influencing the progress of the epidemic. When the many factors so far in doubt are gradually made known, it will be possible to attack the entomological side of the question with better promise of success. Among the unknown factors which cause the greatest confusion in interpreting epidemiological evidence are (1) the length of the period of incubation; (2) the number of mild, abortive or unrecognizable cases and carriers of the virus and their relation to infection and immunity; (3) the duration of infectivity in clinically recognized cases; (4) positive knowledge of the presence of the infective agent in insects, domestic animals or other possible intermediate hosts or reservoirs of the virus.

The "Standardization" of Market Milk.—"Standardized" or "adjusted" milk is attracting much attention at the present time. VAN SLYKE (*Circular No. 56, New York Agricultural Experiment Station*) defines standardized milk as follows: "Standardized milk or adjusted

milk is milk in which the original fat content has been changed, and also the ratio of fat to the other milk solids by the removal of milk-fat or by the addition of skim milk or by the addition of cream." All who have devoted any thought to the subject of adjusted or standardized milk are agreed (1) that promiscuous, uncontrolled standardization should not be considered under any circumstances; (2) that if such treatment of milk is permitted it should be controlled by law as completely as practicable; (3) that this must be done in order to prevent the obviously objectionable conditions which would result from lack of such control. Among the more important conditions that would be necessary to make standardization safe, Van Slyke recommends that no one should be permitted to prepare standardized milk for market purposes without a special State license; that such conditions of standardizing processes should be prescribed as would ensure no impairment of the sanitary quality of the milk. He further recommends that standardized milk should not be permitted to be sold unless it conforms with the legal minimum requirements in composition; that all containers of such milk should be marked with the words "Standardized" or "Adjusted." He also believes that it is all-important to place on every container of standardized or adjusted milk in plain figures the minimum percentage of fat in milk, which shall stand as a guarantee that the milk in the container contains no less than the specified amount of milk-fat. This would serve as a check to prevent adjusting the fat of market milk down close to the present legal minimum standard of 3 per cent. (in New York). It would enable every consumer of such milk to know the minimum percentage of fat in each lot of milk purchased. It would protect distributors and producers against unfair competition, it would have the tendency of helping to adjust or standardize the price of market milk in accordance with the composition of the milk furnished, and, more important still, the successful employment of such a method would probably have the ultimate effect of making the sale of milk on a guaranteed fat basis supersede entirely the present minimum legal standard method for all kinds of milk, whether normal or adjusted.

Total Symblepharon.—MORAX (*Ann. d'Oculist.*, cliv, 321) observes that whereas partial symblepharon can generally be managed readily, such is not the case in total symblepharon with complete abolition of a conjunctival sac. The formation of a new cavity for prosthesis is a most difficult problem. The tendency to retraction and contraction of the orbital tissues is such that the most extensive and perfect graft suffers retraction such that the new cavity decreases greatly and may even disappear almost entirely. To obviate this tendency the author has devised a procedure which consists essentially in the formation of two wide "trap-doors," the raw surfaces of which are turned outward above and below by suturing their edges to the skin after freshening the latter. Wide epidermal grafts from the arm, thigh or abdominal wall are then applied to the raw surfaces. At the end of about three weeks the "trap-doors" are replaced and sutured together at their free margins after freshening. A shell of lead or enamel is placed and allowed to remain between the doors and the bottom of the cavity now covered with the graft. At the expiration of from six weeks to three months

the palpebral margins are cut and prothesis is possible. Several illustrations show the conditions before and after operation and three diagrams assist in making the descriptions clear. The same procedure is applicable where the orbital cavity is still occupied by a globe or stump.

Melanoblastomas of the Eye.—FOREMAN and HUGGER (*Am. Jour. Ophthalm.*, February, 1918, 97) present a study of these tumors of the choroid. They may be either primary or secondary; the former are the more frequent, and the large majority of these are composed of pigment-producing cells. The pigment-bearing choroidal tumors are usually referred to as melanosarcomas. In this region pigment-free tumors are sometimes observed which differ in nowise either in structure or clinical course from those which contain pigment. Such tumors have been termed leukosarcoma, an unfortunate term because it has been used to designate cases of definite tumor-like mass composed of lymphoid cells, which seem to escape into the blood stream, giving rise to leukemic alterations in the blood. The writers adopt the comprehensive term of melanoblastoma as a suitable group name for all tumors composed either of melanoblasts or chromatophores; it has the advantage of not placing any emphasis upon benign or malignant forms, thus compelling a more careful study and evacuation of individual cases. Marshall in his collection of 134 cases of melanosarcoma of the eye (*Royal London Ophth. Hosp. Rep.*, v, xv, 51) found that the ages ranged from fifteen to ninety years, with an average of fifty years. One eye is affected, as a rule. The cases on record appear to be equally divided between the right and the left eye. Injury is considered an important etiological factor by some authors. In Marshall's series there was a definite history of injury in about 10 per cent. Among the 55 eye specimens in the Museum of Pathology at the Ohio State University, upon which this study is based, there are 4 cases of melanoblastomas arising in the eye. These cases are quite fully detailed from the clinical and pathological stand-point. Case 2 is a study of the liver in an instance of melanosarcoma—the eye had been removed on account of a tumor which the reporters did not have the opportunity of studying, though it seems certain that this tumor was the primary growth, the liver and also the lungs being favorite seats of metastases.

Utility of the Tonometer of Schiötz in Practice.—MARBAIX (*Ann. d'Oculist.*, January, 1918, 27) believes that this instrument gives greater precision than the finger, showing degrees of hypertension which would escape the latter; it has drawn attention specially to moderate degrees of hypertension, 30 to 40 mm., which have been found to occur during the course of quite a number of affections, such as iritis, scleritis, myopia, desceminitis, retinal hemorrhages, the appreciation of which may lead to modification in treatment. The instrument is quite applicable, especially in glaucoma, in which the subject remains for a long time under observation and may readily be made to comprehend the importance of repeated examinations. In fact, in the case of any ocular infection in which digital exploration raises a suspicion of a modification in the tension the tonometer should be a real and valuable adjunct in practice.

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

EMERITUS PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

The Morbid Anatomy of War Injuries of the Ear.—J. S. and J. FRASER (*Journal of Laryngology, Rhinology, and Otolology*). From this paper the authors exclude those cases of hysterical deafness or deaf-mutism and malingered deafness which have been treated *in extenso* by Moure, of Bordeaux, Lermoyes and other writers, and include direct injuries due to bullets or pieces of shrapnel or high-explosive shell; indirect injury due to blow or falls on the head, these being subdivided into those with and those without fracture of the labyrinth capsule; noise deafness due to prolonged or intense gunfire, and shell or explosion deafness the consequence of a concussion of the labyrinth. In the cases of direct injuries, fractures of the mastoid process or of the external bony canal were observed, some with and some without splintering of the bone; in some of these cases the tympanum and the labyrinth were also involved and the middle and external ear were in other cases injured by bullets entering through the facial bones and emerging through the mastoid or remaining embedded in the temporal bone, the nature of the injury being determined by radiograms, both lateral and anteroposterior, many of the cases of direct injury being complicated subsequently by middle-ear suppuration occurring as the result of infection carried in by the foreign body at the time of the injury or consequent upon secondary infection through the tympanopharyngeal tube or external canal. Indirect injuries of the ear due to fractures at the base of the skull, similar to those reported by one of the authors as occurring in civil life, were also observed, in one case a bullet wound of the frontoparietal region being accompanied by laceration of the brain and hemorrhage into the subarachnoid space. Noise deafness is due to physiological overstimulation of the auditory apparatus, and the author's conclusions are in consonance with the experiments of Siegman and others that the air-conduction of the sound is of paramount importance in the causation of this physiological condition, conduction of the sound waves through the tissue of the body being relatively unimportant. The hair cells of the organ of Corti are first affected, later the supporting cells, and finally the ganglion cells and nerve fibers, constituting a degenerative neuritis, the part of the organ of Corti affected depending, as has been shown by experiments on animals by other observers, on the pitch of the sound. If the noise be of high pitch the neuro-epithelium at the base of the cochlea is involved; if the noise be of medium pitch the organ of Corti in the middle coil is affected, while if the noise is of low pitch, degeneration is found in the portion of the organ of Corti nearer the apex of the cochlea. It is difficult or impossible to draw the line between cases of

noise deafness and those of shell or explosion deafness, as both are due to the excessive movement of the atmosphere conveyed to the labyrinth, the explosion of a shell not only causing a great mass movement of air but producing a loud noise. It is stated, however, that the blow produced by the condensation of air following the explosion reaches the ear before the noise of vibration, and that it may drive the stapes inward and fix it in the oval window so as to lessen the bad effect of the loud noise which follows. Shell or explosion deafness, concussion of the labyrinth, is, according to Lermoyes, the true war deafness, and various theories have been advanced as to the pathology of this condition. In many cases a rupture of the tympanic membrane accompanied by hemorrhage is observable, and it is believed that in these cases of localized injury there is less likelihood of damage to the delicate structure of the membranous labyrinth than in cases in which the tympanic membrane does not give way; mere rupture of the drum-head, however, unless accompanied by some lesion in the labyrinth, auditory nerve or brain, would produce only a moderate diminution of hearing, while patients suffering from severe shell deafness exhibit marked or total loss of hearing, and in these cases some further lesion in the auditory apparatus must be sought. It has been stated that hemorrhages occur in the peri- or endolymphatic spaces of the inner ear, and that the delicate neuro-epithelial sacs and tubes of the membranous labyrinth are ruptured by the violent concussion caused by the explosion, and that in this way a gross mechanical effect is produced in the inner ear. It would appear, however, that the structures of the membranous labyrinth are well protected from concussion because they are suspended in a lymph bath inside the hollow spaces of the bony labyrinth. Hemorrhage may also occur in the internal auditory meatus with or without rupture of the nerve fibers which pass from the fundus of the meatus through the rigid bony canals to the cochlea, utricle, saccule and cristæ of the canals. It has been suggested that, apart from these gross mechanical changes, the explosion and the loud noise may destroy the delicate nerve-endings in the cochlea and so result in paralysis. The loud sound due to the explosion may paralyze the hair cells of the organ of Corti, somewhat in the same way as the nerve structures of the macula in the retina are paralyzed by the rays of the sun in eclipse blindness. According to this theory shell deafness, like noise deafness, is due to paresis or paralysis following overstimulation. Microscopic examination in one case of labyrinth concussion followed by total deafness exhibited a condition of degenerative neuritis similar to that described by Manasse and Wittmaack in old people. It has also been stated that in cases of shell deafness the lesions are probably to be found in the brain—hemorrhages in the pons, medulla and cerebellum, involving the central connections of the auditory and vestibular nerves, shell deafness having, according to this view, a similar pathology to cases of concussion of the brain in which there is no fracture of the skull, namely, multiple small hemorrhages. Investigations of the authors, including 4 cases of shell or explosion deafness. In each case the temporal bone on the injured side having been removed within four or five hours of death, properly protected and prepared for microscopic examination. The first case was one of shrapnel injury of the left ear followed by middle-ear suppuration, and when admitted to the Royal

Infirmary, Edinburgh, about a month after the injury, symptoms of cerebellar abscess were present. Operation revealed mastoiditis and small metallic particles in the mastoid antrum, and in spite of the evacuation of the cerebellar abscess the patient died. The autopsy showed early meningitis and sinus thrombosis in addition to the cerebellar abscess. Microscopic examination of the ear demonstrated a thickened, infiltrated and perforated drum-head with fracture of the malleus, the lower part of the handle being separated from the drum-head and drawn inward by the tensor tympani muscle. The mucosa of the middle ear was distinctly swollen and the tympanic cavity, antrum and cells full of pus. The joint between the head of the malleus and the body of the incus was dislocated. The incostapedial joint was healthy, but there was fracture of the footplate of the stapes and early invasion of the vestibule through the annular ligament. The cochlea showed hemorrhage in the scala tympani of the basal and middle coil and in the opening of the perilymphatic aqueduct, but the nerve apparatus of the cochlea appeared almost healthy. The neuro-epithelium of the saccule and utricle and of the cristæ of the canals was desquamating. The internal meatus showed meningitis. The second case was one of indirect injury to the ear, due to a bullet wound, the patient having been hit in the frontoparietal region and the bullet going out just above the ear on the same side. There was no apparent injury of the ear itself, but the parietal bone was shattered and the brain lacerated. The third case was that of a soldier who was taking cover in a house when a high-explosive shell hit the house and burst into the room in which he was, the patient being wounded in many places. On admission to the casualty clearing station the patient was found to be semiconscious, with subnormal temperature, small, rapid pulse, cold, clammy skin and multiple small wounds, showing the usual signs of high-explosive shell injury, including marked deafness. He died twenty-four hours later from shock, there being found on examination rupture of the tympanic membrane, slight hemorrhage in the middle ear spaces and in the fundus of the internal auditory meatus, the structures of the membranous labyrinth remaining normal. The fourth case was an injury to the ear due to the bursting of a rifle grenade. The grenade burst close to the left side of the soldier and caused extensive general injury. These rifle grenades, though much smaller than shells, contain a very powerful form of high explosive. The changes in this case were fairly definite and include a recent rupture of the tympanic membrane, the edges of which were partially glued together by fibrin and hemorrhages in the tympanic cavity, in the marrow spaces in the roof of this cavity and around the geniculate ganglion, and in the fossa subarcuata. There was also bleeding in the scala tympani of the cochlea, in the region of the round window, and a marked hemorrhage in the fundus of the internal meatus. The otolith membrane of the saccule was separated and the neuro-epithelium was irregular, with the cupola of the superior canal also separated. Although the outline of the organ of Corti was preserved the hair cells and some of the supporting cells could not be made out, changes probably due to a degenerative neuritis of the nerve structures. In this case the stress of the explosion had been exerted on the posterior inferior part of the drum-head, the region of the round window, and the fundus of the internal auditory meatus.

Case V was one of shell explosion, the patient suffering from severe concussion and the right side of the head and body presenting multiple wounds. There was a plug of wax in the right external auditory canal, and after its removal the right drum-head was found to be lusterless, opaque and retracted. The internal changes in this case were found to be comparatively slight, due possibly to the protective effect of the presence of the rumen plug in the external canal. There were small hemorrhages in the tubal part of the tympanic cavity, in the canal of the tensor tympani, in the cranial ends of the fossa subarcuata and perilymphatic aqueduct and in the fundus of the internal meatus. The neuro-epithelium of the labyrinth showed little change, but the detachment of the otolith membrane of the utricle and of the cupulæ of the lateral and superior canals is worth recording. In Case VI the soldier had caught the full blast of a high-explosive shell, which burst close to his left side and shattered this side from head to foot, the force of the explosion, however, having been expended in rupturing the drumhead, the structure of the inner ear together with the nerves in the internal meatus having correspondingly escaped. The only changes of importance found in the 4 cases of explosion injury of the ear were: rupture of the drum-head and hemorrhage into the middle-ear spaces, with hemorrhage in the fundus of the internal meatus in 3 of the 4 cases.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

Investigation of Strains of Tubercle Bacilli from Animal Tuberculosis.

—GRIFFITHS (*Journal of Pathology and Bacteriology*) reports the results of experimental work carried on from 1911 to 1916, in which he examined a number of strains of the tubercle bacilli from naturally acquired tuberculosis in animals. Out of 14 strains derived from 10 monkeys, 50 per cent. yielded tubercle bacilli of bovine type, this proportion being much higher than that reported by other observers who found in 37 naturally tuberculous monkeys only 3 (8.1 per cent.) were infected with bovine tubercle bacilli. That so many naturally tuberculous monkeys should have yielded the bovine type is not surprising when it is remembered that monkeys are as susceptible to bovine as to human tubercle bacilli, and when in captivity are frequently fed on cows' milk. But an interesting fact in the majority of "bovine" cases here reported is that the infection appeared to be of respiratory origin, the intestines and mesenteric glands showing only minor lesions, if any. The other animals examined were one cat, one goat and seven birds. The cat, a domestic pet, was found to be infected with a typically bovine type, infection being by way of the alimentary tract. The goat, purchased

for experimental purposes, reacted to the tuberculin test and so was killed and examined. A culture obtained from a lung nodule exhibited the characteristics of the bovine type of tubercle bacillus. This is apparently the only case of natural tuberculosis in the goat in which the type of bacillus has been determined. The seven birds examined comprised a lap-wing, a pigeon, a goshawk, an ibis, a quail, a grackle and a pheasant. All the strains exhibited the characteristic cultural features of the avian type of tubercle bacillus. Griffith included in his report the results of an investigation of the cultural characteristics of a series of strains of bovine tubercle bacilli derived from cows' milk. Twenty-eight strains were examined by him and the findings compared with those of the Royal Commission on Tuberculosis. All possessed the same characteristics, *i. e.*, they varied as to their mode of growth on glycerin media, some being very dysgonic, others relatively eugonic and others displayed intermediate degrees of luxuriance. Another interesting finding incorporated in this report is that of a newly calved heifer, two and one-third years old, vaccinated when four days old with living human tubercle bacilli. Upon examination of the first milk produced a virulent strain of the human type was demonstrated. At autopsy, with the exception of a single minute gray tubercle in the lungs, no sign of tuberculosis was found anywhere in the body. The purpose of this investigation was not so much to show the efficacy of vaccination as to draw immediate attention to the possible danger of using for human consumption the milk of cows which had been vaccinated with living human tubercle bacilli.

The Pathology of Gas Gangrene of Muscle.—EMRYS-ROBERTS and COWELL (*Journal of Pathology and Bacteriology*) recognize three types of gas gangrene clinically: (1) the common type which occurs in the wounded lying out twelve to twenty-four hours or which develops a few hours after the first operation; (2) the fulminating type, in which the patient, if untreated, may be dead in a few hours; (3) the delayed type, with a slow onset so that the condition becomes established several days or even weeks after the date of injury. They emphasize that the formation of gas in the common type is a late phenomenon, that changes in the skin overlying the infected wound precede it; the pallor of the tense skin is followed by a reddish blush, soon becoming a dusky violet, which spreads rapidly from the edge of the wound. Before this the constitutional signs of toxemia are present. The fulminating type of gas infection is favored in gross gunshot injuries of bones, with extensive laceration of muscles, and when the main blood supply to a limb has been completely lost the infection is favored by the presence of the symptom-complex of shock, hemorrhage and exhaustion. From observations on the power of *Bacillus aërogenes capsulatus* to produce gas in anaërobic media and from their experiments the authors are persuaded that acid is one of the manifestations of its growth in muscle and that acid hematin is responsible for the initial color changes. Gas gangrene is especially liable to occur in deep penetrating wounds and in extensive surface wounds with great laceration of muscle and containing infective material. There is no actual pus on the wound surface, although a sanious, foul-smelling fluid escapes and a thick, turbid

lymph may be seen in the fascial sheaths. At first the surface is hard to the touch, but as the infection spreads, softening occurs and crepitation may be determined. Histologically the superficial necrotic muscle is composed of swollen fragmented fibers with separated perifibrillar sheaths embedded in a fibrous reticulum, in whose meshes are a large number of polymorphonuclear leukocytes, bacteria, red blood cells and débris. Some small blood clots lie in this area and examination showed them to be crowded with *Bacillus aërogenes capsulatus*, so that it is important to remove these so far as possible. Thrombosis of the vessels quickly occurs and their musculature undergoes lytic changes. In the area of dead muscle the color runs through reds to grays and greens and black. The tissue is no longer contractile. Gas forms late and pushes along the planes of fascia and pressure from this, in the case of such muscle as the tibialis posticus, with rigid fascial compartment, may be sufficient to partially occlude the main vessels. The gas may later burst into the muscle and find its way into the subcutaneous tissue. The authors found that massive thrombosis, apart from that resulting from trauma, is not concomitant of the process of gas gangrene. Histologically, in this area, myolysis was very general and the authors believe that this is due to the toxin of the organism. A fibrinous reticulum with its enmeshed leukocytes is less noticeable in the direction of spreading edge, its place being taken by fluid. The line of demarcation between living and dead muscle fibers is not sharp. Contractility of muscles returns in this area. In the area in which the muscle is contractile some of it may contain extensive blood extravasations. As regards the mode of spread of gangrene it occurs within the fascial sheath; thus the infection is confined to the affected muscle unless the main blood supply is interfered with or unless the exudate, tracking along the sheaths of arteries, nerves and tendons extends the process from one segment to another. In corroboration of this, authors record the case of a man whose penetrating shell wound of the thigh was opened twelve hours after being hit, and who, on the next morning, had constitutional signs of infection and a tympanitic thigh, the wound having the typical odor. The infection was found limited to the sartorius alone. Resection of the whole of this muscle was followed by recovery. In the line of demarcation a white line of fibrin and leukocytes abuts against the contractile muscle. Sloughing sometimes occurs at this line. The authors agree with Emery that toxins produced by the growth of these anaërobes and not the gas are the chief factors in the production of gangrene.

A Method for Producing a Rapid Immunity to Pneumococci.— Much attention has been given to the development of an active immunity to the pneumococcus. Attempts have been made to develop large quantities of antibody in animals for use as diagnostic and therapeutic sera. Various methods that have been used were developed by the individual investigators according to their conception of the important factors entering into the question of stimulating immune substances by pneumococci. ALEXANDER (*Jour. Med. Res.*, 1918, xxxvii, 471) undertook the investigation on the assumption that the immunity in pneumonia was related not alone to the presence of the pneumococcus but also to a reaction of the leukocytes. Pneumococci and leukocytes

were mixed together and incubated for a certain length of time. The mixtures were then used as antigens and injected into rabbits, whose sera were tested for the presence of protective substances. The pneumococcus type II was used in the experiments. The organism was sensitized with immune serum, agglutinated and mixed in definite numbers with leukocytes. After incubation of the mixture it was inoculated intravenously into rabbits. Three daily injections were made and the blood was then tested six to eight days after the last injection. The rabbit serum was tested for protective substances in the white mouse. In this way a potent antipneumococcus serum was rapidly obtained in rabbits. Although ordinarily the rabbit is very susceptible to pneumococcus infection it was found that the sensitized pneumococcus mixed with leukocytes permitted the employment of large doses. The author did not study the manner of effect of the leukocytes upon the pneumococci. He particularly draws attention to the speed with which the protective substances appear in the serum of the treated animal.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,
WASHINGTON, D. C.

A Study of the Physical Condition of One Thousand Delinquents Seen in Court.—ANDERSON and LEONARD (*Boston Med. and Surg. Jour.*, June 13, 1918), state that the original purpose of their study was to determine what part, if any, routine physical examination might play in the disposition of a delinquent's case in court, and later in the institution of reconstructive measures while on probation. For this purpose the records of the last 1000 cases were taken from the files and the last physical condition of each person noted; also the relationship, if any, which the physical condition bore to his economic efficiency. Six hundred sixty-eight individuals, or 66.8 per cent. of the cases, were in good or fair health; 342 individuals, or 34.2 per cent.—1 out of every 3 persons—were in poor or bad health, and in such physical condition as to warrant urgent medical treatment. About 626, or 62.6 per cent., were considered self-supporting, while 374, or 37.4 per cent., were not self-supporting. Some correlation between these figures is evident. Thirty-five per cent. of those found to be in good or fair physical condition had been steadily employed, while only 2 per cent. of those found to be in poor or bad physical condition had been steadily employed. Eighty-five per cent. of those found to be in good or fair

physical condition had been and still were self-supporting, while only 18 per cent. of those found to be in poor or bad physical condition had been and were still self-supporting. The chances for being self-supporting were more than four to one in favor of the individual in good physical condition. Additional facts are included bearing upon the frequency of venereal disease among a group of 600 consecutive cases studied. Forty-seven per cent. of these individuals were suffering from one or both of these diseases; an additional 4.5 per cent. had doubtful bloods and smears. Of these 600 cases, 303 were so-called offenders against elasticity; of these, 57.4 per cent. were suffering from syphilis or gonorrhoea, or both, while an additional 4.9 per cent. were doubtful cases. There were 112 cases of larceny. Of these individuals, 33.9 per cent., or 1 out of every 3 cases, had syphilis or gonorrhoea, or both. There were 17 individuals arrested for possession of drugs; 53 per cent. of these had venereal disease. Other types of offenders in court showed a correspondingly high frequency of these conditions. In short, the conclusion reached from this study is that venereal diseases is not limited to any one type of offender in court, but it is found common among all classes of delinquents, and that a policy calling for a more routine investigation of the physical condition and the possibilities of each offender prior to his disposition would seem justifiable.

The Growth-promoting Properties of Foods Derived from Corn and Wheat.—VOEGTLIN and MYERS (*Public Health Reports*, May 31, 1918, No. 22, xxxiii) state that the "highly milled" products are, without exception, inferior in dietary value, as regards growth, to foods prepared from the whole grain. It is rather surprising that such delicate organs as the gastro-intestinal tract of young mice can tolerate a diet containing a large amount of bran. This fact, however, does not necessarily mean that it is advantageous to include the bran in foods intended for human nutrition. On the contrary, the experiences with "war bread" would rather indicate that persons with delicate digestion are subject to temporary digestive disturbances as a result of a change from "white" bread to bread containing a considerable percentage of bran ("war bread"). On the other hand, from the stand-point of dietary completeness, a bread containing all of the grain, with the exception of the superficial cellulose layer, is undoubtedly superior to the so-called white bread made from "highly milled" flour, and would not possess the above-mentioned features. The "white" bread used in these experiments was not adequate for maintaining normal growth in spite of the fact that it was prepared with some evaporated milk and yeast. The most significant defect of "white" flour is the deficiency in antineuritic and fat-soluble vitamin; it is also deficient in adequate protein and inorganic salts. A wheat flour containing a considerable part of the germ and superficial layers of the grain supports growth of mice and pigeons specially well when supplemented with inorganic salts. The same is true of "whole wheat" bread. "Highly milled" corn-grits, forming the exclusive food of young hogs, leads to failure of growth in these animals, whereas the whole corn-kernel, supplemented by inorganic salts, promotes growth. Newborn squabs are suitable animals for growth experiments. No evidence of a toxic action of a whole-wheat diet was obtained in the experiments on squabs which were fed on whole wheat meal,

supplemented by a suitable salt mixture. In the light of our present knowledge it would appear that bread made from "whole-wheat" flour, or old-fashioned cornmeal, should be used in preference to "white" bread and "highly milled" corn foods whenever the diet is restricted to these cereal foods to the more or less complete exclusion of other foods possessing greater dietary values.

The Influence of Cold Shock in the Sterilization of Canned Foods.—BUSHNELL (*Jour. Ind. and Eng. Chemistry*, June, 1918, No. 6, x) states that blanching is of no value in reducing the time necessary to properly process canned foods. Small amounts of salt are of little value in preventing the growth of bacteria in canned foods. Small amounts of organic acid (acetic acid) have a distinctly retarding action upon the growth of bacteria in canned vegetables. The use of small amounts should be advocated in all cases in which it will not injure the texture, flavor or appearance of the product. In many cases an unsterile product will keep indefinitely if properly sealed. This, however, is not true in all cases, and sealing should not be expected to take place of proper processing because of the danger of loss due to spore-forming anaërobes.

A Comparison of the Relative Healthfulness of Certain Cities in the United States Based upon the Study of Their Vital Statistics.—HARMON (*Quarterly Publication of American Statistical Association*, June, 1916) states that the use of a life table furnishes the best single means of comparing communities in regard to their health. The use of standardized death-rates constitutes the next best method, and it is much to be preferred to the use of the crude death-rates. The infant mortality rate is not a satisfactory index of the health of the community, because in most instances there is no accurate method of expressing it. The death-rates from the various infectious diseases do not give comparable results. The death-rate from a single disease apparently does not give a just and fair representation of the healthfulness of a city. In judging the healthfulness of a city, such rates should therefore be used with care and discretion.

Elementary Concepts of Tuberculosis.—KRAUSE (*Am. Rev. of Tuberculosis*, April, 1918, No. 2, ii), states that from three to five years to twelve to fifteen is the golden age of the human span so far as tuberculosis is concerned. At this period the disease is milder than at any other time of life. It is astonishing how many of the apparently desperately sick children will recover from tuberculosis. As in infancy, generalized miliary or meningeal tuberculosis will carry off most of those who die. But if these complications do not develop the immediate outlook is uniformly good. However, cured children furnish many of the chronic pulmonary cases of adult life. Even though cured, such children should be looked upon as cripples. Therefore, whenever possible their future life should be planned with this conception firmly in mind. They must concentrate their talents if they are to be useful members of society and free from tuberculosis. The treatment of tuberculosis does not stop with the arrest of symptoms. A well person's life may have to be watched perhaps for years in order to ward off relapse and prevent an ultimate death from phthisis.

Wound Inspection among Lathe Workers.—SHEE (*Jour. Am. Med. Assn.*, lxi, 1927-1930) states that in a large manufacturing plant the vast majority of cases of wound infections and furunculosis were found to be localized among lathe workers in the machine shops. The peculiar features of lathe work are the use of cutting mixture and oil, and the manner in which these circulate and are used repeatedly, thus making them extremely liable to contamination. The contamination rendered them open to suspicion as factors in the causation of the wound infection and furunculosis. These suspicions were borne out by bacteriological investigation and animal inoculation, which showed the causative factor to be pyogenic organisms which were present in vast numbers in the cutting mixture and less numerous in the oil. Marked results were obtained. Abundant portals of entry for these organisms were found on the arms of workmen in innumerable small cuts and punctures made by flying chips of steel from the lathes. The methods of prophylaxis possible are by heat, by chemical disinfection and by a combination of the two. Various chemical disinfectants were tried, and the cresol group was found to be the most effective and the least expensive. By use of chemical disinfection (cresols) wound infections have been reduced from 5 per cent. to less than 0.5 per cent. in the plant under consideration, and furunculosis has almost disappeared.

An Anatomical Study of Senescence in Dogs, with Special Reference to the Relation of Cellular Changes of Age to Tumors.—GOODPASTURE (*Jour. Med. Research*, May, 1918, pp. 127-186) states that senescence in dogs is accompanied by multiple degenerative changes in many organs and tissues, and associated with these changes are multiple benign and malignant tumors, which seem to result directly from these degenerative changes. With age there is a progressive differentiation which eventually injures the cells of the body. Many of these cells die, others become de-differentiated in varying degrees. These de-differentiated cells possess the power to grow, but their capacity to function may be diminished or lost. From these de-differentiated cells, metaplasia and benign and malignant tumors arise.

Persistence of Immunity following Toxin-antitoxin Injections.—PARK (*Proc. Soc. for Exp. Biol. and Med.*, April 8, 1918), during the past years, has immunized a series of guinea-pigs and a series of horses and a series of children, with diphtheria toxin-antitoxin mixtures. The duration of the immunity presents certain points of great interest. He states that, so far as his observations go, guinea-pigs are never naturally immune; horses in the very great majority of cases are immune; adults and infants under six months are immune to 80 per cent., while very young children are non-immune to about 60 per cent. In the guinea-pig, active immunity lasts for about nine months; in horses there is increased immunity, due to the injections, which last from nine to twelve months, at which time the horses return to their original amounts of natural antitoxic immunity. In testing human beings from month to month it was a matter of great interest to find whether the infants and children who become immune, due to the injections, would, like the guinea-pigs, lose their immunity in about

nine months or whether the active immunity would be replaced by natural immunity just as in the majority of infants the stage of lack of immunity is followed by antitoxic immunity. He found that in infants two years after successful immunization the great majority have remained immune, not over 6 per cent. losing their immunity. Park states that we have a right therefore to hope that the stimulated immunity has been replaced in the very great majority by a natural immunity, and that this will hold for life. The facts that the protection lasts and that the injections are harmless make the active immunization of infants appear to be a practical measure of eliminating diphtheria.

The Spirochetal Flora of the Normal Male Genitalia.—NOGUCHI (*Jour. Exp. Med.*, June 1, 1918, No. 6, xxvii), states that the varieties of spirochetes enumerated and photomicrographed from the male smegma flora represent practically every form hitherto described by Nankivell and Sundell and by Patterson in the specimens of urine from trench fever cases. The urethral flora as studied by Stoddard seem to contain more varieties, but except those of his more detailed morphological descriptions, every form observed by him is among those found in the smegma. Stoddard saw certain forms with hooked ends suggestive of the *Leptospira icterohemorrhagiæ* of infectious jaundice, but the resemblance ends with this one feature, and differentiation should always be possible under the dark-field microscope, by means of which spirals the leptospira reveals its highly characteristic minute elementary presenting the appearance of a chain of dots. Of all the spirochetes none has so closely set spirals as the jaundice leptospira, the distance between two spirals being only 0.5 micron. Various methods, including Fontana's, Benians', the mordant gentian violet stain or Burri's India-ink method, are inadequate to differentiate the leptospira from other spirochetes. Why a positive spirochete finding with the films from the urethra and in the specimens of urine was not obtained is difficult to explain, except on the grounds of the paucity of specimens examined. At all events the recent negative results reported by Fiessinger with French soldiers and invalids after cleansing of the urethra and glands seem to be in harmony with Noguchi's results. In conclusion it may be stated that *Spironema refringens*, *Treponema calligyrum* and *Treponema minutum* represent practically all the spirochetal forms observed in the male smegma flora. A leptospira has never been conclusively shown to be present in the specimens of normal urine or smegma. For the satisfactory microscopic demonstration of a leptospira a dark-field illuminator is indispensable.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

SEPTEMBER, 1918

ORIGINAL ARTICLES

**FOCAL NECROSIS OF THE ADRENAL GLAND: WITH REMARKS
UPON ACUTE ADRENAL INSUFFICIENCY.**

BY ELI MOSCHCOWITZ, M.D.,

PATHOLOGIST TO THE BETH ISRAEL HOSPITAL, NEW YORK CITY.

INTRODUCTION. The lesion is an unusual one. While it has been reported many times, the descriptions have been meager and often inaccurate. Indeed, I have been unable to find a single graphic representation of this lesion in the literature. Moreover, it has never been described as a distinct and unalloyed lesion of the adrenal, and, in consequence, has thus far been nameless. The name I have suggested fits the morphological characteristics accurately; indeed, the resemblance to the more familiar focal necroses of the liver is a very close one. These facts, it seems to me, warrant the purpose of this study, which is based upon two cases observed within a short time.

The study of these two cases led inevitably to an examination of the clinical features of acute adrenal insufficiency, a phase that is always associated, and, moreover, is paramount in nearly all the contributions to the study of this lesion. The reports are so diverse and confusing that it seemed wise at the same time to submit a critique of this aspect as well.

CASE I.—H. B., aged forty-one years, male. Admitted October 26, 1913. Three weeks before admission the patient complained of headache, distress in the epigastrium and in the precordium, weakness and anorexia. He had relief for a few days, then the symptoms returned, especially the intense headache. Patient was

dizzy, had flashes before his eyes and there was puffing of forehead and face. The urine showed a trace of albumin and gave a positive test with the guaiac reaction. Roentgen-ray report on October 27, 1913, shows a calculus in the left kidney.

Operation, November 10. Right nephrectomy by Dr. Goodman. Pathological report: Calculous pyelonephritis. Patient was returned to bed in profound shock; pulse, 146. Intravenous infusion given.

November 11. Pulse, 112, poor in quality; temperature, 96 to 97.4°; respiration, 14.

November 12. 8 A.M., pulse, 80; respiration, 16. 12 M., temperature, 93.6°; respiration, 8. 6 P.M., temperature, 93.6°; respiration, 10. 9 P.M., temperature, 96°; respiration, 20. 11 P.M., temperature, 96; respiration, 20.

November 13. Ceased to breathe.

Report on Removed Kidney. The kidney is about twice the normal size; granular surface; capsule not adherent. The pelvis is enormously dilated and congested. It is coated with exudate in many areas and contains bloody purulent urine and one large free stone. The parenchyma of the kidney is pale red; markings poor; cut surface markedly granular; papillæ much flattened.

Microscopically. There is an abundant growth of new connective tissue between the tubules in all stages of organization. The tubules are dilated; the epithelium is flat, granular and stains poorly. Many of the tubules contain hyaline cylinders and fresh blood, especially in the straight papillæ. The glomeruli are fairly well preserved, somewhat contracted; within many of the capsules is a fine granular material. The lining squamous epithelium of the pelvis is well preserved; here and there it is covered by fresh exudate. There is a notable increase of the round cells beneath the epithelium. Diagnosis: calculous pyelonephritis.

Autopsy. Lungs, heart and right adrenal not removed.

Left Kidney. About twice normal size. Surface smooth; dark brownish red. There are numerous punctate, hemorrhagic spots the size of a pinhead. On section, deeply congested; cortex thickened; markings clear; glomeruli easily visible.

Spleen. Normal.

Pancreas. Normal.

Aorta. Moderate atheroma.

Adrenal. Very large, distinct capsule, white center, surrounded by hemorrhagic fat.

Anatomical Diagnosis. Compensatory hypertrophy of kidney, with acute congestion.

Microscopic Examination. *Kidney*. Hemorrhages in tubules; slight edema of stroma; moderate parenchymatous nephritis.

Spleen. Normal.

Pancreas. Normal.

Aorta. Small amount of lime in media.

Adrenal (Fig. 1). Larger than normal and embedded in hemorrhagic tissue.

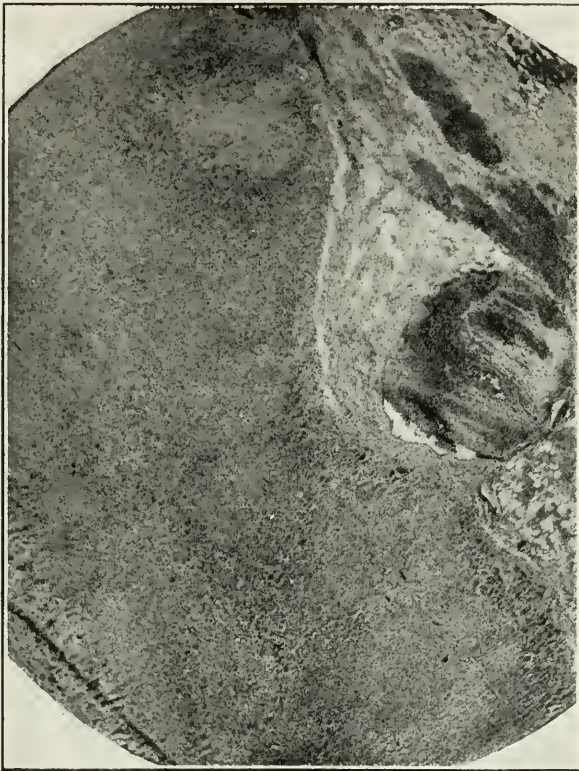


FIG. 1.—Low-power appearance of adrenal from Case I, showing a number of areas of focal necrosis in the cortex and thrombi in the capsular vessels.

With the low power there are perhaps a dozen or more foci where the normal parenchyma of the organ has been manifestly destroyed. These areas are distinctly circumscribed from the surrounding parenchyma and take little or no hematoxylin stain. The majority of these foci have a hemorrhagic appearance, due to the presence of masses of red blood cells. These foci are uniformly round; some are confluent and exist exclusively in the cortex. The medulla is intact. As a rule there is a thin rim of cortex between the foci and the surface of the organ, although some extend to the very surface itself. The majority of these foci have a honey-combed appearance, due to the presence of well-preserved strands of intertrabecular connective tissue.

Upon studying these foci with the high objective (Fig. 2) we find the adrenal tissue has been almost completely destroyed; that

parenchyma cells are mere "shadows" without nuclei or very pale ones. They have entirely lost their normal arrangement and stain deeply with eosin. In some foci no trace of parenchyma whatever is visible, being replaced by a pale acellular tissue resembling fat. Scattered throughout these foci are abundant polymorphonuclear cells. In some foci these are so abundant as to almost warrant the term abscess. The polymorphonuclear cells are distributed evenly throughout the foci; in some, and especially those that reveal the

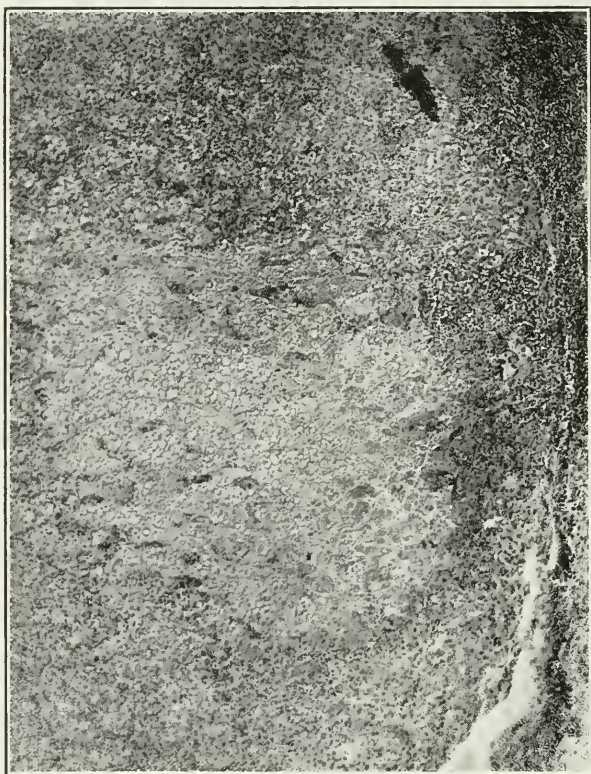


FIG. 2.—High power of one of the focal necroses, showing intense parenchymatous degeneration and peripheral polymorphonuclear infiltration.

most profound necrosis, the polymorphonuclear cells are densely arranged around the circumference of the focus. These foci also contain abundant red cells. These cells are sometimes distributed haphazardly, as in a hemorrhage. In some areas they are present within dilated capillaries. In addition to these three cellular elements—namely, destroyed parenchymatous cells, polymorphonuclear leukocytes and red blood cells—we find in these foci a fourth element—namely, radially arranged strands of the intertrabecular connective tissue—which give the honey-combed appear-

ance described above. These strands are especially abundant near the periphery of the foci, becoming absent in the central portions.

The parenchyma of the organ between and surroundings these foci are very well preserved. There is some engorgement of the cortical capillaries, and in the medulla a few of the veins are filled with a red thrombus.

The connective-tissue capsule of the adrenal is normal.

The fatty and connective tissue immediately surrounding the organ, however, is intensely hemorrhagic. Especially noteworthy is the uniform presence of hemorrhagic and mixed thrombi in the vessels. The vessels appear greatly dilated and are either completely or nearly completely filled with thrombus consisting of fibrin, with a greater or lesser admixture of red blood cells. The intima is completely absent wherever the thrombus is in contact with the wall of the vessel, but there is nowhere evidence of beginning organization.

Summary. A man, aged forty-one years, with calculous pyelonephritis. Nephrectomy was done. Promptly after the operation the patient went into profound shock. After an intravenous infusion he rallied so that on the following day his pulse was 112, although firm in quality. For the remaining two days of his life his temperatures were subnormal, 93.6° to 96° F., with normal pulse rate and decreased frequency of respiration.

CASE II.—Jennie G., aged eight years, was admitted to the Beth Israel Hospital January 1, 1916. Her parents and their four other children were alive and well.

The child had been nursed until one year of age. She had suffered from a chronic cough from the eleventh month until the end of the second year, when she had a severe attack of measles. During the fourth year it was noticed that the child's abdomen became enormously enlarged and that she steadily lost weight. At that time Dr. Hymanson suspected tuberculous peritonitis, although the temperature was normal and the von Pirquet test was negative. The parents would not permit tapping of the abdomen. On prolonged use of tonics, with creosote, together with good nourishment, the child gained weight, and in the course of eighteen months the ascites almost disappeared.

In the month of May, 1914, the child was brought to Dr. Hymanson and the mother told him that for the previous two months the patient had again been losing weight; had had frequent micturition, with milky urine. The child was very anemic, weighed only twenty-eight pounds and some dulness could be detected at the lower part of the abdomen. The urine looked turbid and fibrinous coagula were observed when it stood for some time. By shaking the urine with ether the dissolved fat rose to the surface and the

¹ For the details of the clinical history I am indebted to Dr. Hymanson.

urine became quite clear. Microscopically the fat globules were in a fine state of subdivision. Sudan III stained the fat particles red. No filaria and no blood had been detected. By advising complete rest, involving absence from school, and the administration of salol, urotropin and belladonna there was slow improvement; some weight was gained, and on July 31, 1915, the urine was examined by Dr. Max Kahn, who reported that it contained a huge amount of mucin, but no lactose, fat or casein.

November 27, 1915, the frequent micturition and milky urine reappeared. Dr. D. Constantinides examined the urine and found albumin, 0.365 per cent.; fat, 0.225 per cent.; also some pus cells and epithelium; no sugar. On allowing the urine to stand a cream-like mass of fat rose to the surface.

Condition on Admission. The child was anemic and very emaciated, weighed only thirty-four pounds, was not playful, complained of frequent frontal headache, was nauseated and vomited several times a day. The heart, lungs and abdominal organs were normal; there was some dulness at the lower part of the abdomen and some nodules could be palpated at the right inguinal region. The glands in both groins were also palpable. There was no edema and no cyanosis. The patellar reflexes were somewhat exaggerated. Temperature, 99.4°; pulse, 120; respiration, 28.

A blood examination showed erythrocytes, 3,800,000; total leukocytes, 14,400; polymorphonuclear cells, 70 per cent.; lymphocytes, 30 per cent. There was no eosinophilia. The hemoglobin was 60 per cent. No filaria were found in the blood.

Von Pirquet tests were done twice, with negative results. Wassermann test was also negative. The stools contained no ova or red cells. The guaiac test for sugar was positive.

The urine also contained lecithin and cholesterin.

The microscopic examination of the urine showed many white cells, a few hyaline casts and bladder epithelia, but no filaria. A diagnosis of chyluria was made.

During the first week of the child's stay in the hospital, under the administration of urotropin and sodium benzoate, her condition improved somewhat and at times the urine almost cleared up, but it always contained some fat. Then the temperature began to rise and reached as high as 104.6°. The headache, nausea and anorexia increased in severity, the urine became loaded with pus, was markedly ammoniacal and the fat was increased in quantity. The stools contained some blood. The cervical glands became enlarged, although there was no congestion of the throat, and some ecchymotic spots were noticed all over the body and extremities. The pulse became very weak and at times irregular.

The eyes were examined by Dr. Ervin Török on January 15, who found that the pupils reacted only sluggishly to light. Both disks were covered with a whitish exudate and were moderately swollen.

There were several hemorrhages on and around the disks. The bloodvessels were large and tortuous. Diagnosis: albuminuric retinitis.

A blood culture was negative. The same evening and on the following day the patient had a number of convulsive attacks, which were most marked on the right side of the body. These were controlled by chloroform. A lumbar puncture was done, but the spinal fluid was normal.

On January 17 the patient became comatose and the pulse was at times imperceptible. The cervical glands became more enlarged and death ensued from cardiac failure.

Necropsy. A necropsy was performed on the child eight hours after death. The body was very much emaciated. The cervical, axillary and groin glands were enlarged. Some ecchymotic and petechial spots were noticed over the extremities. The *lungs* were normal except for some slight congestion at the bases. The *heart* was much enlarged, the muscle of the left ventricle being about 2.5 cm. thick, firm and pale. The left ventricle was dilated; the muscle of the right ventricle was 1 cm. thick. The valves were normal, with the exception of a few atheromatous patches on the ventricular surface of the mitral valve. The *liver* was slightly enlarged, and on section was pale, brownish red and cloudy. The *stomach* mucosa was covered with mucus, but otherwise normal. The *right kidney* was 8 x 3 x 2 cm. It was very irregular in contour, showed fetal lobulations, and was fairly firm, with adherent capsule. The surface beneath was very irregular, with numerous depressions and sulci between prominences representing remnants of kidney tissue. These prominences were paler than the surrounding portions, project above the surface, and, on section, were grayish and sharply defined from the surrounding tissue. Section through the kidney proper showed a complete obliteration of all markings, so that it was impossible to differentiate cortex from medulla. The cut section was pale red. There were numerous ecchymoses on the surface, the pelvis was somewhat dilated and the papillæ were flattened. The ureters were somewhat dilated and thickened. The left kidney was 6 x 3 x 2 cm., was somewhat smaller than the right and presented practically the same picture, except for the absence of fetal lobulations. Only the left *adrenal* was removed: it was slightly enlarged, otherwise normal. The pancreas was enlarged. The *spleen* was enlarged and measured 12.5 x 6 x 3 cm. The surface was smooth; it was deep red on section and the pulp was firm. Malpighian bodies were prominent. There was a fresh infarct of a dirty brown color, about the size of a bean, in the lower pole, soft in texture and sharply circumscribed from surrounding tissue. The *intestines* were normal. The *mesenteric lymph* nodes were enlarged. The *bladder* was dilated, the walls being extremely hypertrophied; the mucosa was smooth and presented many ecchymotic areas.

Anatomical Diagnosis. Chyluria; chronic diffuse nephritis (contracted kidney); chronic congestion of lungs; hypertrophy and dilatation of the left ventricle; splenic hyperplasia, with fresh infarct; parenchymatous degeneration of the liver; hypertrophy and dilatation of the bladder; hypertrophy and dilatation of ureters.

Microscopic Examination. Lungs. The epithelium of the bronchi was desquamated and the lumen contained an exudate of polymorphonuclear cells. Around the smaller bronchi the alveoli contained an exudate consisting of polymorphonuclears and round cells. The walls of the alveoli in the remainder of the lung were thickened and the capillaries were markedly dilated. The muscular fibers of the heart were normal and there was no infiltration. The cells of the liver were slightly granular and the nuclei somewhat pale. There was a very moderate amount of fat in the cells.

Spleen. The splenic veins were dilated and filled with blood. The infarct showed profound necrosis, with many "shadow" cells and nuclear detritus. Some of the bloodvessels in the necrosed area were still preserved and contained red thrombi; other vessels showed beginning hyaline degeneration. The splenic veins surrounding the infarct were dilated to an enormous size. The capsule and trabeculae of the spleen were normal.

The pancreas showed a few areas of autodigestion. Scattered here and there throughout the organ were small focal areas of polymorphonuclear infiltrations. In these areas the pancreatic cells stained less deeply than in the remainder of the organ. The islands of Langerhans were normal.

Kidneys. The microscopic picture of the kidneys, even on superficial inspection, showed complete disorganization. The interstitial connective tissue was enormously increased and in areas showed a profound infiltration, with round and plasma cells. The tubules varied greatly in size and in shape; no distinction could be made between any of the various portions of the tubules. The majority of the tubules were dilated and the epithelium was flat and stained poorly. Most of them contain hyaline casts and some of these casts contained polymorphonuclear cells. The glomeruli revealed various forms, some being completely hyaline, some partially so; some contained new connective tissue, others were enormously hypertrophied and others showed a polymorphonuclear infiltration. The Bowman capsules were uniformly intact. A few of the glomeruli contained bacterial thrombi. The capillaries were very prominent and dilated.

The intestines and the mesenteric lymph nodes were normal. In the submucous connective tissue of the bladder there was a marked blood extravasation, but the organ was otherwise normal.

Adrenal (Fig. 3). With the low power the most striking feature is the presence of numerous plugs of bacteria situated immediately beneath the connective-tissue capsule of the adrenal or slightly

beneath it. These plugs are dense and are either perfectly round or sausage-shaped, obviously conforming to the lumen of the capillary in which they are plugged. These plugs exist singly or in groups of two or more, and are usually surrounded by a comparatively small number of polymorphonuclear leukocytes. Many plugs, however, are not surrounded by any reactive zone of leukocytes whatever. On the other hand, we find numerous focal, small collections of leukocytes in which no bacterial plugs can be demon-

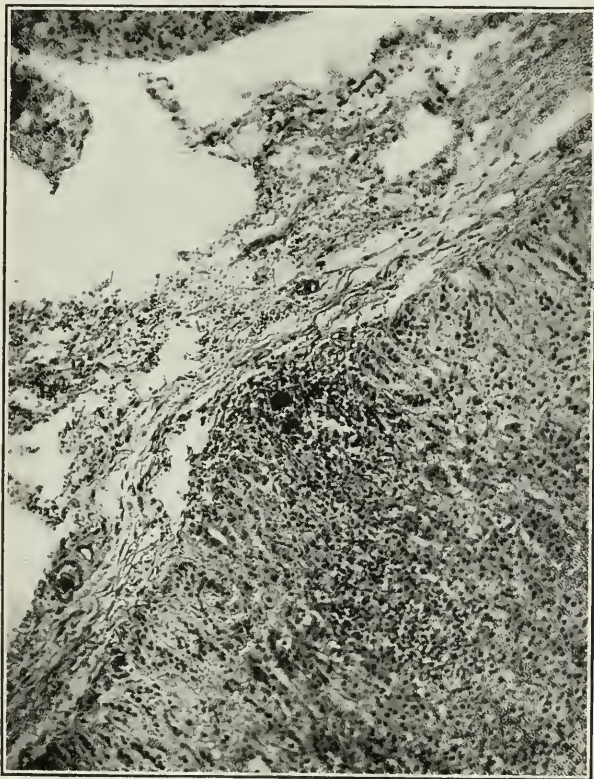


FIG. 3.—Section from adrenal Case II, showing bacterial infarct in cortex with slight polymorphonuclear infiltration.

strated (Fig. 4). Some of these focal collections of leukocytes surround a small area of necrotic adrenal tissue, as evidenced by "shadow cells," as in the previous case. The polymorphonuclear infiltration affects the intertrabecular connective tissue.

The capillaries of the adrenal are engorged and here and there is a small ecchymosis. With the exception of a lighter stain than normal the parenchyma of the adrenal is normal.

The connective tissue surrounding the organ shows considerable extravasation of blood. The vessels show no change whatever.

Incidence of Focal Necrosis of the Adrenal. In an examination of many hundreds of adrenals, these are the only two that have shown definite evidence of an inflammatory lesion. My autopsy experience in infectious diseases, it must be confessed, has been rather limited.

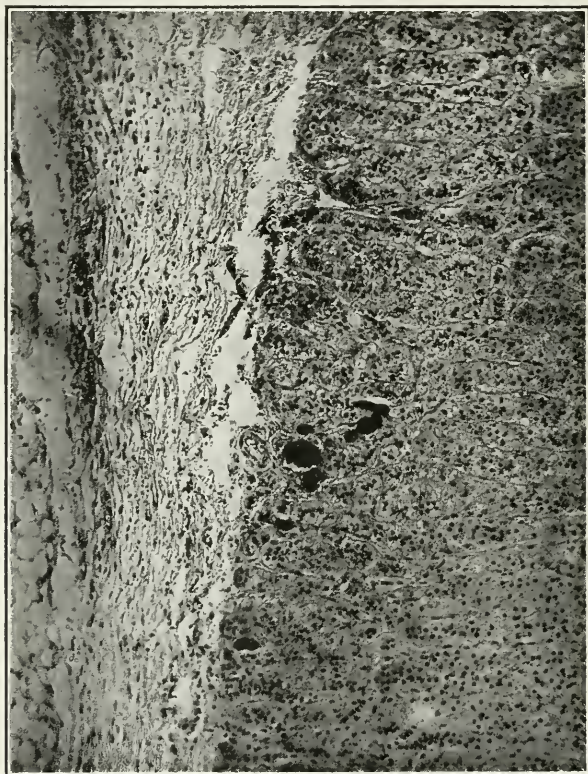


FIG. 4.—Section from adrenal Case II, showing bacterial infarcts in cortex, with practically no polymorphonuclear infiltration.

A study of the literature, on the other hand, confers the impression that inflammatory changes in the adrenal of human beings are not uncommon, although the data are too few to gauge the precise incidence. Babes² in a series of 150 consecutive autopsies found acute lesions of the adrenal in 25 cases. In 11 there was hyperemia, with disappearance of fat, sometimes associated with small hemorrhages in the gland and infiltration of the capsule. In these cases one finds foci of polymorphonuclears or mononuclears, with degeneration or necrosis of the parenchyma. In 14 cases of infectious disease Babes found foci of bacteria in the cortex unas-

² Compt. rend. Soc. de biol., 1908, lxx, 235.

sociated with secondary inflammatory reaction. Marchetti,³ in a series of 1200 autopsies, describes congestion and hemorrhage of the adrenals in the infectious diseases. Goldschmidt,⁴ in a study of 53 adrenals in all kinds of diseases, found lymphocytic infiltration in infectious diseases and evidences of phagocytosis in the cortex cells resembling in appearance the 'Russel bodies' found in malignant tumors. Ziegler⁵ says that small foci of inflammation may occur in the infectious diseases which may pass into suppuration and subsequent scar formation. Aschoff⁶ describes edema of the adrenal in infectious diseases as common. Rarer are embolic foci in the cortical zone resulting in "herdförmige" acute inflammations. From these, he says, miliary or even larger abscesses may form. Scheel⁷ describes edema of the interstitial tissue of the adrenals as a frequent occurrence in febrile disorders. Neusser and Wiesel⁸ say that acute inflammations of the adrenals are not rare; these occur most often in the form of edema and parenchymatous degenerations. He describes focal necroses as occurring in severe infections, especially in diphtheria. Loeper and Oppenheim⁹ noted very small leukocytic infiltrations in bronchopneumonia of children, and in streptococcus infections. These same authors¹⁰ have found inflammatory lesions in diphtheria, variola, typhoid and tetanus. They mostly found parenchymatous changes. Focal necroses they noted only in diphtheria. In other diseases, areas of necroses are found, but these are not the direct result of the toxin but are due to hemorrhages. Occasionally they found polymorphonuclear infiltrations of the adrenal. Oppenheim¹¹ describes cases of dysentery in which, at autopsy, the adrenals were large and congested, with cellular necroses and hemorrhages. Beitzke¹² finds bacterial emboli in the adrenal frequently; often this lesion is the only site of bacterial embolism found at autopsy.

Experimental Acute Inflammatory Lesions of the Adrenal. Much work has been done, especially by the French school, to obtain lesions of the adrenals in animals by the injection of pathogenic bacteria. As far back as 1889 Roux and Yersin¹³ found degeneration of the adrenal in experiments in diphtheria. Langlois and Charrin¹⁴ found congestion and hemorrhages in the adrenal after pyocyanus infections. The most comprehensive experimental

³ Virchows Arch. f. path. Anat., 1904, clxxvii, 227.

⁴ Deutsch. Arch. f. klin. Med., 1909-1910, lxxxviii, 186.

⁵ Specielle Pathologie, Jena, 1906, 11te Aufl.

⁶ Ibid., Jena, 1912, 2te Aufl.

⁷ Virchows Arch. f. path. Anat., 1908, clxxxii, 494.

⁸ Erkrankungen der Nebennieren, Leipzig, 1910, 2te Aufl.

⁹ Manuel des Maladies des Rein, edited by Dehove, Archard and Castaigne.

¹⁰ Loeper and Oppenheim: Arch. de expér. et d'anat. path., 1901, xiii, 683.

¹¹ Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, xxxix, 1155.

¹² Berl. klin. Wchnschr., 1909, xlvi, 2, 769.

¹³ Ann. de l'Inst. Pasteur, 1888, ii, 629; 1889, iii, 273.

¹⁴ Compt. rend. Soc. de biol., 1893, p. 812.

studies are those of Oppenheim and Loeper,¹⁵ who obtained lesions in diphtheria, tetanus, anthrax, and pneumococcus infections. They describe hemorrhages, infiltration with leukocytes, parenchymatous degenerations and necrotic foci; the latter are especially characteristic in diphtheria infections. They found the lesions most often in the reticular and fascicular zones of the gland. Labsin¹⁶ found degenerations and hemorrhages of the adrenals in rabbits and in dogs after injection of streptococci. Crowe and Wislocki¹⁷ found necrotic foci in the adrenal cortex of animals after acute general infections.

These observations upon human beings and animals indicate that inflammatory lesions of the adrenals are not uncommon in the infectious diseases. It would seem that they occur more frequently in experimental bacterial infections than in human beings. Also that such lesions are more common and more profound in diphtheria than in any other infection.

Varieties of Lesions of Adrenals Associated with Infections. As we have seen the lesions of the adrenal associated with infections are various. They may be grouped in the following manner: (1) Parenchymatous degenerations; (2) edema of the interstitial connective tissue; (3) hemorrhages; (4) infiltration with leukocytes; (5) focal necroses; (6) bacterial emboli, with or without secondary inflammatory reaction; (7) miliary or larger abscess. Of these the most common are parenchymatous degenerations and hemorrhages. While some writers, especially those that have written textbooks (Ziegler, Aschoff, Kauffmann, and Beneke¹⁸) speak of abscesses of the adrenal as not a strange phenomenon, I have been able to find but 3 authentic cases, those of Chvostek,¹⁹ Janowski,²⁰ and Stursberg.²¹ A curious observation is that made both by Beitzke and Simmonds,²² who found cortical bacterial emboli associated, with parenchymatous degeneration, as the only evidence of bacterial embolism as part of a general infection in the body.

Pathogenesis. So far as available data permits us to judge the lesions in the adrenals may result either from a general toxic action (degenerations, hemorrhages, necroses) or from the action of bacteria themselves (bacterial emboli, abscesses). It seems curious that I have been able to find but few cases of an inflammatory lesion occurring in the medulla of the organ. The lesions that I have described seem to occur mostly in the cortex. Crowe and Wislocki confirmed this observation in their extensive experiments upon

¹⁵ Arch. de méd. expér. et d'anat. path., 1901, xiii, 332.

¹⁶ Arch. de soc. biol. de Petrograd, 1905, xi, 319.

¹⁷ Beitr. z. klin. Chir., 1914, xcv, 8.

¹⁸ Zülzer's Klin. Hand. der Harn. u. sexual organs, Leipzig, 1894.

¹⁹ Wien. med. Presse, 1880, p. 1425.

²⁰ Gaz. lek., 1898, liv, 354.

²¹ Deutsch. med. Wchrschr., 1904, xxx, 1406.

²² Virchows Arch. f. path. Anat., 1898, clxxii.

acute and chronic infections in animals. The only explanation of this phenomenon I can offer is the peculiar blood supply of the adrenal gland. According to Henle, numerous small arteries from the periphery penetrate into the fibrous capsule of the gland, where they form an anastomosing plexus. These small arteries then penetrate the parenchymal cortex and immediately form capillaries between the cortical columns. From here the blood is collected into small veins in the medulla, whence the blood passes into the adrenal vein. We thus see that bacterial emboli, no matter how small, are promptly caught in the cortical capillaries and have little or no chance to penetrate into the medulla.

If this explanation is valid, the pathogenesis of inflammatory lesions of the adrenal as due to the direct action of bacteria seems the more probable one.

The lesion in my second case is an exquisite example of bacterial embolism.

The lesion in my first case requires a different interpretation. Three explanations are possible:

1. That the lesion was the result of the contagious infection—namely, the pyelonephritis. I do not believe this etiology is probable and for the following reasons: (1) Because it is hard to conceive how an infection of such low grade could cause such an intensely acute lesion. Indeed, so far as I am aware, a focal necrosis in the adrenal has never been observed, either at autopsy or experimentally, in chronic infections. (2) The patient did not reveal any evidence of any grade of general sepsis, either bacterial or toxic.

2. The second explanation is that the lesion may have been due to a postoperation sepsis. Against this explanation is the fact that the patient revealed not the slightest sign of clinical sepsis after the operation.

3. The third explanation, and the one I believe most probable, is that the lesion was due to the peri-adrenal hemorrhage, with consequent thrombosis of the adrenal vessels. My reasons for this belief are: (1) by exclusion of any other factor, and (2) detailed examination of my specimens reveals the fact that the necroses are most abundant in those portions of the adrenals in which the thrombosis of the capsular vessels is most widespread and are correspondingly absent in those portions in which thromboses are absent.

According to this conception the focal necroses in the adrenal may be regarded as infarcts.

Clinical Aspects of Acute Adrenal Insufficiency. The attempt to interpret certain symptoms and signs as due to the obvious interference of function produced by the lesions that I have described is certainly a reasonable endeavor. The French also have been especially active in this field, notably Arnaud, Sergent and Oppen-

heim. Arnaud's²³ contribution appears to have been the first in which a systematic attempt was made to set forth the clinical features of acute adrenal insufficiency, and is based on a study of 80 cases in which hemorrhages, from whatever cause, were found in the adrenals at postmortem examination. Significantly enough, in the vast majority of cases no symptoms that could be directly attributed to the adrenal lesion were present. In 5 cases a hematoma of palpable size was present. In 6 cases the symptoms resembled those of an acute peritonitis. In 8 cases symptoms of so-called "adrenal insufficiency," such as muscular asthenia, prostration, vomiting, diarrhea, abdominal pain, hypothermia, syncope and collapse were present. In 15 cases there was sudden death, or death within a few hours, with symptoms of delirium, convulsions, contractures, coma, hypothermia, syncope, etc. Sergeant,²⁴ who has written extensively on the subject, claims to have discovered a pathognomonic sign of acute adrenal insufficiency in the so-called "white line." This sign is obtained by running the finger-nail or pin along the skin, when a white instead of the usual red line will form. This line is supposed to be due to a temporary constriction of the relaxed vessels. He claims that the triad, "white line," hypothermia and asthenia make the diagnosis of acute adrenal insufficiency certain.

Oppenheim describes cases of dysentery in which there was sudden cholera, like collapse, with hypothermia, concave abdomen, small rapid pulse, vomiting and diarrhea. In some instances he obtained the "white line" of Sergeant. At autopsy the adrenals were large and congested, and contained cellular necroses and hemorrhages. Good results were obtained by opotherapy.

Dudgeon,²⁵ in an extensive study of acute adrenal hemorrhages, admits Arnaud's classification and adds two syndromata of his own: (1) cases suggesting an acute specific fever, and (2) cases with severe skin lesions, such as purpura.

Lavenson²⁶ reports the case of a woman, aged forty-four years, who suffered from vomiting, epigastric pain, prostration and delirium. The temperature was 98° and the pulse 48 and imperceptible. There was tenderness in the epigastrium and loins. The predominating symptoms were those of shock. She died thirty-six hours after the onset of the illness. At the autopsy there was an acute pancreatitis. There was thrombosis of the adrenal vein secondary to this lesion. The adrenals were enlarged, soft and red, with necroses of the parenchyma and hemorrhagic extravasations. He believes that the symptoms from which the patient suffered were in part due to the adrenal lesion and classifies the

²³ Arch. gén. de méd., 1900, clxxxvi, 5.

²⁴ L'Insuffisance surrénale, Paris, 1902.

²⁵ Am. Jour. Med. Sc., 1904, cxxvii, 134.

²⁶ Arch. Int. Med., 1908, ii, 62.

recorded cases into the following five types: (1) the asthenic form; (2) cases in which symptoms of shock are present, associated with gastro-intestinal symptoms, bradycardia, lumbar pains and death; (3) cases of sudden death; (4) nervous type, with convulsions, coma and delirium; (5) cases associated with purpuric lesions within the abdominal cavity.

Riesman,²⁷ basing his observations upon Lavenson's report, reports 5 cases of "adrenal insufficiency." The main symptoms were physical weakness amounting to actual prostration, a feeling of coldness, subnormal temperature, slow pulse and low blood-pressure. As all the patients recovered there were no postmortems.

Williams²⁸ describes cases of neurasthenia or psychasthenia with such symptoms as weakness, low blood-pressure and pigmentation of the mucous membranes. Some die and others recover under opotherapy. He believes that some of these cases may arise after periods of hyperfunction of the adrenals due to mental strain (Cannon).

It cannot be said that the protean and conflicting observations thus far adduced afford a sense of satisfaction, as indices of an acute adrenal insufficiency. Indeed, these form adequate grounds for a critique from many aspects.

In the first place we must remember that the presence of a lesion in an organ, even of such profound physiological import as the adrenal, does not necessarily signify that the lesion gives rise to clinical symptoms. For instance, we know that profound degenerations and almost complete destruction of these organs by metastatic tumors may occur without the slightest evidences of Addison's disease (Kaufmann²⁹). Specially significant in this connection are the observations of Arnaud, which we have already quoted, who found that out of 80 cases of adrenal hemorrhage studied, in 46 no symptoms had been present. Obviously the absence of clinical symptoms in cases in which a profound lesion of the adrenal is found at autopsy may be explained in one of two ways: (1) that in many such cases the lesion is unilateral, so that the remaining adrenal assumes the entire physiological function; (2) in cases in which both adrenals are affected, detached portions of unaffected adrenal tissue may be present in the neighborhood or distant parts of the body (*e. g.*, broad ligament, spermatic cord). In any event the absence of symptoms where lesions of the adrenals are present is sufficiently common to make hazardous a clinical deduction based upon pathological findings.

In the second place the function of the adrenal gland is a complex one. The adrenal gland, physiologically speaking, cannot be regarded as a single organ with a single function. Rather it must

²⁷ Jour. Am. Med. Assn., 1912, lviii, 1846.

²⁸ *Ibid.*, 1914, lxiii, 2, 2203.

²⁹ Lehrbuch der path. Anat., Berlin, 1911, 6th auf.

be regarded as a dual organ, consisting of a medulla and a cortex, each of different embryological origin and each possessing different physiological functions. So far as the physiology of the adrenal has been worked out the cortex functionates to neutralize toxins, bears an obscure relation to the formation of pigment and to the development of some of the secondary sexual characteristics. The medulla, on the other hand, maintains the vascular tone by the elaboration of adrenalin and bears some relation to sugar metabolism. If any of these functions are diminished or absent we could not logically diagnose disease of the whole gland but only of a portion. When we consider, furthermore, that these functions are dependent to a greater or lesser degree upon the activities of other endocrine organs, notably the islands of Langerhans, the thyroid and the pituitary, we can readily understand how difficult it is to create a more or less precise symptom-complex from a disorder of the adrenal function. Certainly the various forms of symptoms-complex that we have quoted bear little relation to the physiology of the organ as we have outlined it. Even in Addison's disease, when the relation of the symptoms to disease of the adrenals has been fairly well established, it is a question as to how far the symptoms, with the exception of the pigmentation, and possibly of the asthenia, are due to the actual involvement of the adrenal gland. Finally, we must remember that the underlying infection causing the adrenal lesion is in itself capable of causing symptoms sufficiently profound to mask or at least modify any possible symptoms arising from involvement of the adrenal gland.

Nor can we accept, without hesitancy, the *post hoc propter hoc* argument of opotherapy as advocated by many. In the first place, adrenalin is only one of the many products of the internal secretion of the adrenal. Even if we admit that it is the most important of the products, it seems illogical to conclude that the administration of adrenalin will save life when we know that at the same time disease of the equally vital essential cortex coexists. Furthermore, the fallacy of judging the life-saving effects of a drug of such unspecific character as adrenalin in conditions that frequently result in cure by other means are obvious.

It seems to me that the only method whereby we may determine clinical acute (and even chronic) adrenal insufficiency is by means of a physiological test. As adrenalin is the only internal secretion of the organ for which we have fairly approximate tests it is logical to assume that the quantity of adrenalin in the blood is a fair index of adrenal insufficiency, provided, of course, that the medulla of the adrenal is assumed to be involved. The clinical possibilities of carrying out such tests was shown by Whipple.³⁰ Using the physiological test of Elliot and the more accurate chemical test of

³⁰ Jour. Exp. Med., xix, 536.

Folin, Whipple found that in acute experimental intoxications in dogs the adrenal index is low; anesthesia and chloroform poisoning cause a marked drop; in pernicious anemia there is an increase. In acute infections (typhoid, sepsis, peritonitis, etc.) the adrenal index is either normal or slightly below normal. In cases associated with high blood-pressure the index is normal or slightly subnormal.

A more direct method of determining adrenal insufficiency would be by determining the adrenal index direct from the gland itself. This was done in one case by Cooke³¹ in a man acutely ill with delirium and general twitchings. Death occurred two days after the onset. At the autopsy both adrenals were caseous. With the physiological test Cooke found a diminution of adrenalin not only in the diseased areas but also in those portions that appeared normal.

SIDE-LIGHTS ON MULTIPLE MYELOMA.

BY ARTHUR WILLIAM MEYER, M.D.,

AND

ROBERT E. SWAIN, PH.D.,

STANFORD MEDICAL SCHOOL.¹

I LIKE to observe the old saying, "Let not the cobbler judge above his last," but even a cobbler should, I presume, keep his eyes open. I was prompted also to make this report because pathologists, when doing necropsies, usually can make only a partial examination of the skeleton. Hence there are exceedingly few extended and probably no complete skeletal surveys on multiple myeloma in the literature. Then, too, although pathologists are not agreed upon what is and what is not a myeloma, the series of cases is still small. While reporting a case, MacCallum (1901) also spoke of the still rather limited series of cases. Bombhard (1914) was able to find a series of 54 cases without, however, trying to discriminate between the metastatic and the non-metastatic. Since this series of 54 cases contains a number with metastases to other organs than the bones and cartilages, the actual number of cases of restricted multiple myeloma is undoubtedly considerably smaller. In addition to these 54 cases the references before me would seem to show that 6 more cases were reported in 1914 and two in 1915 and perhaps 1 in 1916.

It is not often that a case of this intensely interesting condition comes to the attention of the anatomist, and when it does he usually

³¹ Arch. Int. Med., 1912, ix, 108.

¹ The anatomical and chemical portions of this paper were written respectively by Meyer and Swain.

is unaware of the condition until the dissection has progressed fairly well. It is a strange comment upon our management of charitable institutions that this should be so. In case of the body here referred to no information but the data contained on the certificate of death were obtainable even upon subsequent inquiry. These data merely included the name, age, birthplace, occupation of the deceased and the date, the place and the cause of death. The latter, with some justification, was given as "chronic valvular disease of the heart," but the myelomatous condition was apparently completely overlooked.

The body was that of a native of Ireland, aged seventy-one years. It had been preserved in the way customary here, and dissection was begun approximately two years after death. There was no marked evidence of senility or any pronounced emaciation in spite of the very extensive disease shown by the presence of 82 skeletal lesions outside of small foci that may have been contained in the marrow and certain questionable osseous lesions. This number is unique, for although Bender (1902) says that every bone, without exception, was affected in his case, this statement is not supported by his own autopsy report. It is not at all unlikely, to be sure, that some case in the literature upon which only a partial necropsy was made may actually have been affected to a greater extent. But that, too, must remain a matter of conjecture.

A rather marked dorsal kyphosis and also a marked right dorsal scoliosis, with slight compensatory lumbar scoliosis, were present in this cadaver. Similar spinal curvatures are also noted in the literature, notably by Bender (1902). Aside from small nodular prominences on several ribs which might have been due to old calluses from fractures, there was nothing to attract special attention to the body except a marked defect in the sternum. Upon palpation a yielding, softened area was found to extend from the lower third of the manubrium to the third rib. A nodular prominence, about 1.5 x 1 x 0.5 cm. in size, was present at the second costosternal articulation, and upon further examination defects were also found in the shafts of the right fourth, sixth and ninth ribs and another several centimeters long near the head of the ninth rib. A similar defect was also noticed at the same point on the left second rib; others at the mammillary line of the left fourth, at the costochondral junctions of the left fifth and sixth and near the angle in the left eighth and ninth ribs.

Upon further dissection it was seen that the trachea was displaced to the right directly cranial to the thoracic aperture and that the innominate artery was prominent, dilated and rather sclerotic. The aortic arch and thoracic aorta were decidedly dilated, extremely sclerotic and calcified. Martiri (1915) also mentions the presence of a pulsating tumor at the base of the sternum and a dilatation of the arch revealed by the roentgen rays. The heart was hyper-

trophied and the left ventricle dilated, but the valves were not sclerotic and looked competent. The rest of the pleura looked normal except for the presence of large partly calcified cartilaginous plaques in the left parietal pleura. One of these lay in the parasternal region opposite the third and fourth ribs. It was 3 mm. thick, 9 cm. long and 5 cm. wide, with the long diameter parallel to the ribs and molded by the latter so that they lay in grooves partly embedded in the plaque. Both pleura and plaques were easily detachable from the thoracic fascia. A similar plaque, 10 x 6 cm. in area and 3 mm. thick, lay on the left dome of the diaphragm, conforming entirely to its curvature. It was roughly oval in shape, with the long dimensions directed transversely. Another plaque lay in the left costal pleura just lateral to the vertebral column, touching the aorta in the region of the eighth to twelfth ribs. It measured 12 x 6 cm., the long dimension lying parallel to the spine. This plaque was triangular, with the apex directed cranially. All three plaques showed some calcification, but looked mainly cartilaginous in gross nature.

Bender (1902) found calcium deposited in zones surrounding the small capillaries of the lung and also in other tissues, and Blatherwick (1916) also spoke of a diffuse infiltration of calcium salts in the lung as revealed by the roentgen rays. Bender, who discusses the so-called calcium metastases in a case of lymphosarcoma and myeloma, says that they occur first in connective tissue, in elastic fibers and in the so-called structureless membranes. All higher organized tissues, such as epithelia, endothelia and smooth muscle, are said to remain free unless they degenerate. Bender concluded, however, that in any case calcium is never deposited in sound tissues and that elastic fibers are the seat of predilection.

The appearance of the connective-tissue framework in the large calcified pleural plaques of this case is shown in Fig. 1. In these specimens apparently all the fasciculi of fibers as well as the interstices of the framework were occupied by calcium deposits.

Except for a dilated bladder and a pronounced hydronephrosis, with marked renal atrophy, especially on the right and probable secondary infection of the kidney and bladder, nothing in the abdominal cavity requires special mention. The spinal arachnoid and pia were decidedly thickened and adherent and the former also contained several small areas of calcification. The dura seemed normal, but the small tumor, about 1 x 0.75 x 0.5 cm., was located in the upper left frontal region about 3 cm. from the midline. It was but very slightly prominent and the dura over it was stripped very easily and was not thickened. Aside from enlargement in the inguinal region the lymph nodes were normal in gross appearance. The fifth right toe was unusually small, pointed and stiff.

As the dissection progressed it was evident that numerous lesions of the bones were present. The ascending ramus of the

right pubis was represented by a thickened, somewhat irregular mass, which had a hard, roughened surface, but yielded on pressure. A slightly prominent, enlarged, soft, circular mass was also seen near the midpoint of the iliac crests. That on the right measured 5 x 4 x 1.5 cm. and that on the left 4 x 3 x 1.75 cm. Similar masses were also seen on the left sides of the bodies of the second and eleventh vertebræ. The head of the twelfth rib was practically destroyed, but the eleventh rib did not seem to be affected. Another large tumor was found on the right dorsolateral region of the body of the eighth dorsal vertebra. This likewise had practically destroyed the head of the corresponding rib. The right halves of the bodies of the first, fourth and fifth lumbar vertebræ were represented by similar tumors which, however, did not seem to invade the intravertebral disks. A still larger mass was contained in the upper right portion of the sacrum.



FIG. 1.—Connective-tissue stroma in one of the calcified pleural plaques. Magnification, 375.

A large tumor, about 3.5 cm. in size, was found below the right glenoid cavity, and this directed attention to a most interesting condition in the right humeroscapular articulation. The subdeltoid bursa was normal, the joint capsule intact, but slightly thickened superiorly, and the long head of the biceps unaffected. But on opening the joint a large pyramidal defect was seen in the superior anterior articular surface of the humeral head. Bombhard states that in the case reported by Herz the head of the right humerus was almost completely destroyed and in Bender's (1902) case the head of the right humerus was also affected.

The inferior two-thirds of the glenoid cavity was represented by a thin remnant of this portion of the articular cartilage only.

This remnant was displaced backward some distance, so as to permit the remaining portion of the scapular head to fit into the humeral defect. The subscapular bursa was much enlarged and apparently filled with a granular mass. It measured 3.5 cm. in length, 2 cm. in width and 1 cm. in thickness. Upon opening it the contents were seen to be composed of 6 grams of ground-up bone and fibrous remnants, which looked not unlike sawdust. Blood-clot or exudate was not present and the bursa still communicated with the articular cavity, which contained many villi.

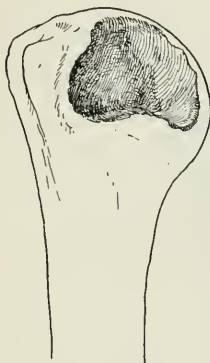


FIG. 2.—Defect in right humeral head, one-half natural size.



FIG. 3.—Defects in the right scapula, one-third natural size.

Upon further examination it was found that the myeloma below the scapular head had destroyed two-thirds of the head, neck and articular surface of the scapula, leaving only the thin cartilaginous disk mentioned above, which was only several millimeters thick. Nevertheless, the original articular surface was still preserved. Smaller tumors were also noticed at the base of the scapular spine, and a larger one, about 3 x 2.5 cm., on the lateral surface near the inferior angle. The cartilage of the remainder of the humeral head was roughened, atrophied and partly eroded, except for a rim about 0.5 cm. wide near the periphery of the head. The defect in the humeral head measured 3.5 cm. across at the base, 3 cm. in a vertical direction and 1.5 cm. in a direction transverse to the head and to the midpoint of its base. Connective tissue from the capsule had proliferated over the anterior margin of the defect, very small portions of the anterior extent of which seem to be covered by cartilage while other small portions are polished (Figs. 2 and 3).

Although all the tumors seemed to be confined to the bones, a careful inspection of all the other organs was made, but not a single lesion was found outside of the skeleton, including the cartilages.

The tendency seems to be to reject those cases in which metastases occur to other organs than the bones or ossified cartilages from the class of true myelomata. Borst (1902) also emphasizes this aspect of the disease. However, Christian (1907) states that Lubarsch (1906) thinks that metastases to other organs are possible. Nevertheless, Lubarsch writes very explicitly, "Ich stehe somit auch auf dem Standpunkt dass das Myelom keine Metastasen macht" (Lubarsch (1906), s. 217). Bombhard (1914) says his case supports either view, and adds that in several instances metastases have even been reported in the muscles. One of Christian's cases and likewise one of Hoffman's also had metastasized to other organs than the bones and cartilages.



FIG. 4.—Exostoses on the distal extremities of the fibulæ.

Next to the very large and numerous defects and tumors and the deformed phalanges the thing that attracted attention to the skeleton was the presence of a general roughening on the cleaned bones, which was very pronounced in the fibulæ. This was due to the presence of plaques, spicules and larger spines or to scores of small sharp exostoses. This roughening was not present on the entire surfaces of the bones, however, and often looked more like a calcareous deposit than like true bone. It was present as plaques over practically the whole of the middle and posterior cerebral fossæ, but practically absent on the rest of the internal and external

surfaces of the skull. The clavicles, ribs, spine, and pelvis showed but little of this deposit, but the long bones of the extremities showed somewhat more, especially near their proximal extremities. However, in the case of the fibulæ the roughening formed by masses of small exostoses, up to 0.5 cm. long, was confined largely to the medial and anterior surfaces of the distal halves, as shown in Fig. 4. The ossa calces, too, were roughened quite extensively.

Aschoff also commented on the slight tendency to bone formation, but Bender (1902) says that resorption within the bone is offset by deposition in many places. Bender reported signs of direct ossification of connective tissue and also of indirect bone formation through an intermediate cartilaginous stage.

In several of the cases in the literature it is stated that considerable softening of the bones was present, especially in the vertebra and near the tumors. Bender, too, speaks of osteoid margins, and Borst (1902) says that the diseased bones not only showed much osteoporosis but the softening of a senile osteomalacia as well. In the case referred to by Borst the vertebra could all be cut with a knife. A softening of the bones is mentioned in some other cases also, but was completely absent in the case reported here, except in the immediate proximity of the tumors of the vertebræ. Indeed, there was not only an entire absence of softening but also an entire absence of senile atrophy. This became especially evident upon section of a number of the bones, including some ribs, the calvarium and a group of long bones.

In addition to the more or less general roughening of the bones there was evidence of arthritis. The bodies of most of the vertebra show some lipping, and some of them also possess small polished areas. Both lipping and polishing are present on the articular surfaces between the dens and the atlas. The bodies of the sixth and seventh cervical vertebra are synostosed anteriorly. The bodies of the seventh to twelfth dorsal vertebræ inclusive are likewise synostosed anteriorly by thick knob-like arthritic deposits. The first and second lumbar vertebræ likewise are synostosed, but in this case probably through the formation of new bone in consequence of or in accompaniment with the myelomatous condition. The right coxal bone is synostosed with the sacrum along the superior margin of the sacro-iliac synchondrosis, and some of the interphalangeal articulations are eroded slightly. To what extent the remarkable changes in the phalanges shown in Fig. 5 were due to the myelomatous condition will be considered farther on. The articular surface of the left greater multangular and the corresponding area on the first metacarpal are eroded and polished and the former is decidedly lipped.

In addition to the very marked absorption in the metatarsals and toes shown in Fig. 5, which may be related to the arthritis, marked absorption is present also on the inferior surfaces of the

maxillæ. This absorption is so very pronounced that only a very small low ridge, which anteriorly and anterolaterally is almost imperceptible, marks the boundary between the inferior and lateral surfaces of the left maxilla as shown in Fig. 6. Not even in the most senile skulls in my possession, some of which show the most pronounced absorption and belong to a later decade in life, show such marked absorption in the alveolar region. The other bones of this skeleton, on the other hand, show practically no evidence of senility whatever.



FIG. 5.—Toes and fifth metatarsals and a normal foot.

An examination of the bones shows that the tendency to bilateral symmetry of the lesions was but slight. A number of the lesions in the pelvis were symmetrically located, however, and both scapulæ were affected, although not symmetrically so. In the flat bones the defects when involving the entire thickness of the bones are quite

circular. When they did not involve the entire thickness or when not limited by cartilages, as in case of the vertebræ, they are spherical. The superficial defects are irregular in form and depth as a rule. It was only in case of the costal cartilages that extensions of small processes of the subperichondrial tumors into the interior of the cartilages was noticed. Von Verebely (1906) seems to have reported the only other case in which the cartilages were affected, and said that this fact added a peculiar interest to his case. In the latter case a tumor in the cricoid cartilage almost obstructed the lumen

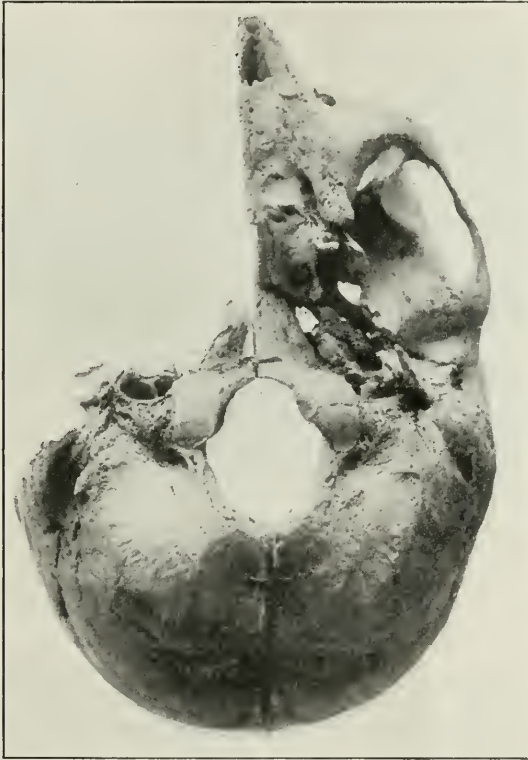


FIG. 6.—Undissected portion of the base of the skull, showing complete partial obliteration of the alveolar process and a superficial lesion on the left articular eminence.

of the larynx. Von Verebely added that the tumors in the larynx and sternum were at first taken for gummata. A deep scar on the glans in the present case similarly misled me, upon inspection of the cadaver when the lesions in the sternum and ribs were first noticed.

Since the costal cartilages showed no ossification the presence of tumors in several of them was very puzzling until examination

showed that small microscopic remnants of bone were still left in the two cartilages affected. Hence it is clear that we are dealing merely with an extension of the disease to areas of previously ossified cartilage. This was also true in the case reported by von Verebély, the only other case in which cartilage was noticed to have been affected. That cartilage is not affected primarily would also seem to be indicated by the entire absence of invasion of any of the intervertebral disks. In typical cases it seems there merely is a protrusion of the tumors through the bone into the surrounding tissues. Bender (1902) states, however, that in his case the tumor cells had invaded the intervertebral disks in certain hemorrhagic areas, and Borst (1902) says that the round cells had infiltrated the inner layers of the periosteum, but adds that it is only rarely that the tumors reach or penetrate the latter. I saw no involvement of the periosteum, although the fibrous trabeculae of the tumors are not infrequently directly continuous with it. This was shown especially well in case of the tumors in the two costal cartilages where extensions from the perichondrium (periosteum?) went directly into the tumor. Very many, in fact most of these 82 tumors, reached the periosteum, however. But even the large tumors which had completely deserted portions of the body of the sternum had not invaded the costal cartilages, although several of the chondrosternal joints were involved. Indeed, the periosteum or the adjacent muscles were involved nowhere and none of the tumor were more than slightly prominent. This was true even of the largest, which measured 4 to 5 cm. across.

The articulated pelvis shows that it yielded under the effect of the body pressure (Fig. 7). Since the right superior ramus of the pubis is completely destroyed for a distance of 3.5 cm. and the ramus of the ischium an equal distance in a line directly below, this need not surprise us. Especially not if we bear in mind that the superior pubic ramus on the left was fractured, and that not only the inferior pubic ramus on this side is almost completely divided, but also the ramus of the left ischium directly opposite the inferior extremity of the obturator foramen. The right coxal bone has been displaced upward, rotating the sacrum to the right. The upper border of the symphysis is directed to the right and lies opposite the right upper anterior sacral foramen.

As one looks at the pelvis it is indeed difficult to see how it could have been possible for the patient to stand with comfort, much less to walk. The lesions are so many, the defects so large and the destruction of important portions of the pelvis so complete that it would seem as though this individual must have been bed-ridden for months. Yet there were no bed-sores, and in the absence of a clinical history the existence of a paraplegia remains purely a matter of surmise, except, perhaps, for the light that the presence of a very pronounced hydronephrosis throws upon this question. Since there

was no obstruction of the ureters it is difficult to see any other explanation for the astonishing atrophy of the renal parenchyma than the presence of a paralyzed bladder. The condition of the latter as well as the great destruction in the lumbar vertebræ and the sacrum, also confirm this supposition. Hence, it would seem that the individual was probably paralyzed in the lower extremities, at least during the later stages of the disease.

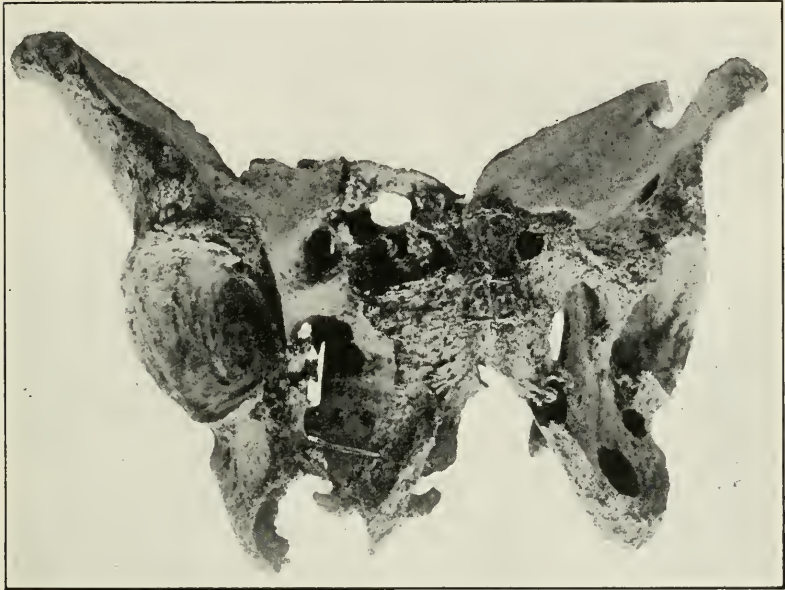


FIG. 7.—Pelvis as seen from the front and right, showing destruction of a considerable portion of the right superior ramus of the pubis and of the ramus of the ischium. The defects are not all visible.

The condition of the phalanges was an exceedingly interesting one and at first sight reminds one somewhat of the atrophy in leprosy as shown by Harbitz (1910). The deformity in the fifth metatarsal, of the first phalanx of the fifth toe and of the second and terminal phalanges of all the toes on the right foot is especially interesting, however. The presence of some deformity in the toes was noticed upon external inspection of the cadaver, but was at first given no further attention, because it seemed more probable that local disease, or accident even, might well be responsible for the curious condition which seemed to exist. The condition of these toes makes one think of arthritis deformans. The absorption of bone is extremely marked, however. The phalanges of the great toe are thoroughly fused and some absorption is evident on the ventral surface.

The terminal and middle phalanges of the second toe must have fused some time before the terminal phalanx was fractured and the distal half displaced plantarly, so as to form an angle of about 80 degrees. These phalanges were united by fibrous tissue, the articular cartilage having been destroyed.

The terminal and middle phalanges of the third toe also had fused. The second phalanx was almost completely absorbed and the middle phalanx rotated 90 degrees counter-clockwise.

The second phalanx of the fourth toe had fused with the first and only a very small remnant of it remained. The terminal phalanx of this toe showed great absorption and the articular surfaces between it and the second phalanx were destroyed.

The first and second phalanges of the fifth toe also were fused and greatly deformed as Fig. 5 shows. The terminal phalanx, on the contrary, was very well preserved, although rotated laterally 90 degrees.

The absorption present in the foot was most pronounced in the fifth right metatarsal. The head of this bone is completely destroyed unless one can consider an irregular process with a very rough articular surface as a remnant of it. The proximal third of the bone is quite well preserved, however, although the plantar surface of the distal three-fourths shows a thin, wide ridge formed by a new deposit. This ridge of bone was 0.5 x 3 cm., and with a much smaller wall medially, included the tendons of the muscles between them. Erosion and polishing were present in a number of these joints.

As shown in Fig. 5 marked absorption was present in some of the second, and especially the terminal phalanges of the left foot also. The second and terminal phalanges of the fourth left toe had fused and the latter was changed into a many-pronged, very irregular process. Some absorption was present also in the first phalanx of the fifth toe.

Old, completely healed, well-united fractures were present in the sixth, seventh and eighth ribs on the right side. These fractures, which are located about in the mammary line, all healed without any displacement and without callus formation, the shafts simply being slightly depressed. The sixth right rib, however, also shows a fracture farther medially. At this point there is a marked callus which looks, however, as though it were due to the presence of a tumor, for the thickening of the bone at this point is specially marked when compared with the slight diffuse thickenings at the other points of fracture. Aside from these fractures, most of which seemed old, there were a few others in the pelvis aside from the one mentioned in the description of the spine and another one indicated in one of the toes. In the superior ramus of the left pubis also an old, well-healed fracture line is clearly visible. There is almost no callus medially and inferiorly at this point and no displacement whatever seems to have occurred, although this fracture was

located just medial to the pectineal eminence. A moderate amount of callus is present superiorly and laterally, however. Another line of fracture, with considerable callus formation, is present in a line directly below, in the inferior ramus of the pubis, where a tumor has left only a thin shell of bone superiorly.

The complete destruction of the superior ramus of the right pubic bone and part of the ramus of the ischium also suggests that fractures were likely present here, although but little callus or new deposit could be found anywhere. Moreover, the displacement and the increased mobility were so slight that the marked destruction at these points did not attract attention until a careful search was made for the other less evident lesions elsewhere. The small amount of callus present is indeed a very striking thing, and the callus, or new bone formation, seems to have been limited very largely to fracture lines, and where more or less motion was inevitable. It is also interesting that as much or even more deposit of new bone, which always looks more like a calcareous deposit than true bone, can also be found in places where no fractures had occurred. However, Aschoff found stalactite formations near old healed fractures in the pubic rami, and Borst emphasized with an exclamation point the fact that some fractures found in his case had healed.

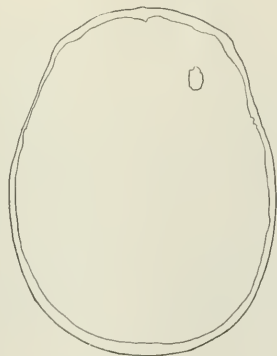


FIG. 8.—Outline of calvarium showing size and location of the lesion, one-third natural size.

SKULL. As noted above, only a single tumor was found in the fresh skull. As shown in Fig. 8 this was located in the upper left frontal region. The defect in the inner table occupied by this tumor has an oval form and measures approximately 1×0.75 cm. This leads into a slightly larger cavity, about 0.5 cm. deep, from which the myeloma was very easily removed. There also is a small superficial defect in the right posterior cerebral fossa and a similar superficial defect in the right cerebellar fossa. There are the only signs of lesions noticeable upon inspection of the interior of the skull.

The exterior seems to be entirely free except for a small superficial excavation on the left articular eminence shown in Fig. 6. This area is about 1 cm. in a transverse and 0.5 cm. in an anterior posterior direction and about 0.5 mm. deep. It is studded with numerous small pits. The appearance of this area can leave no doubt that the destruction here is due to action from the surface.

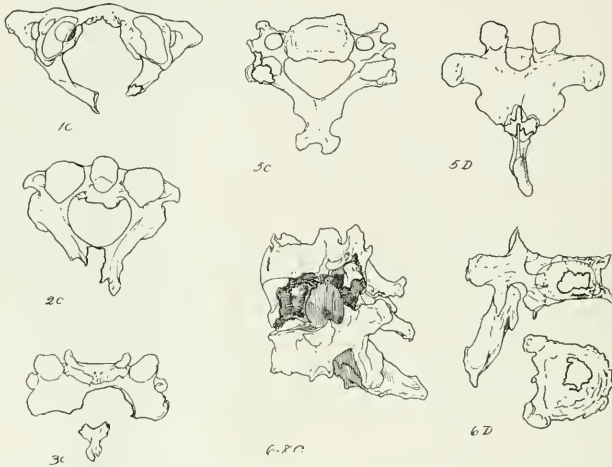


FIG. 9.—Affected cervical and upper six dorsal vertebrae, one-half natural size.

VERTEBRAL COLUMN (Figs. 9 to 12). A small cavity 3 x 4 x 4 mm. deep, open to the surface, is located just dorsal to the tubercle for the left extremity of the transverse ligament of the atlas. The superior portion of this tubercle is perforated by almost a dozen fine canals, about 0.25 mm. in diameter. The articular surface for the dens is decidedly lipped, especially near its superior margin, and most of this area is polished. As shown in Fig. 9 the spine and part of the right arch of the atlas were destroyed.

The left half of the bifurcated spine of the epistropheus and part of its adjoining left arch are destroyed.

The spine of the third cervical vertebra and the adjoining arches are completely severed from the rest of the arch.

The inferior two-thirds of the articular surface of the fifth cervical and the dorsal surface of the base of the arch were invaded for about one-half of their depth, as shown by a roughened excavation about 2 cm. in size.

The base of the left transverse process and the left four-fifths of the body of the seventh cervical vertebra were destroyed.

The spine of the fifth dorsal was almost completely separated at its base and the adjacent arch looked as though the disease had begun superficially here rather than within.

As shown in Fig. 10 the seventh to the eleventh dorsal vertebræ were fused into a single mass by deposits on the ventral surfaces of their bodies and by lipping of the articular surfaces.

A large defect, $2 \times 1\frac{1}{2}$ cm., opens from the dorsal surface of the body of the eighth dorsal vertebra into a large cavity in the interior, so that only a thin outer shell is left of the body of this vertebra. Both pedicles are completely severed and partly destroyed and the spine is affected at about its midpoint.



FIG. 10.—Affected seventh to twelfth dorsal vertebræ, one-half natural size.

An excavation, about $1 \times 1\frac{1}{2} \times 1$ cm., is located on the left side of the body of the ninth dorsal vertebra. The adjacent surface of this vertebra also looks as though it had been affected. The pedicle on the left side is destroyed for almost one-half its width, and there also is a superficial worm-eaten area, about 0.5 cm. wide, at the left margin of the body of this vertebra just caudal to the radix.

The left radix of the tenth vertebra is destroyed almost up to the articular surface. The portion of the body caudal to it has a superficial defect over an area of almost 2 sq. cm.

The greater part of the body of the left radix of the eleventh dorsal vertebra is destroyed. A large defect looks backward and to the left.

The right transverse process of the twelfth dorsal was completely severed and almost destroyed.

As shown in Fig. 11 the defects in the lumbar vertebræ were still greater, for the body of each of these vertebræ is very largely destroyed. The first and second lumbar vertebra are fused, the right two-thirds of the body of the first lumbar vertebra are gone and the right lamina is affected. The left half of the body of the second is likewise destroyed and a superficial oval excavation,

2 x 1 x 0.5 cm., is also found on the left dorsal surface of the body of this vertebra, mediocaudally from the radix. The body of the third is almost completely excavated from its dorsal surface, the cavity reaching the surface, both cranially and caudally, by means of apertures about 1 cm. in size. The right half of the body of the fourth lumbar and the dorsal third of its spine are destroyed. The anterior surface of this vertebra is also denuded of compacta for the entire height of the body over an area about $1\frac{1}{2}$ cm. wide. This denuded area is not more than 2 mm. deep. The right articular process of the fifth lumbar vertebra is detached at its base and the left third of the body is destroyed. The base of the left superior articular process is also affected, the left inferior articular process is detached at its base and the left transverse process destroyed. The right transverse process was fractured and shows some callus formation on its inferior surface.



FIG. 11.—Lumbar vertebrae, one-half natural size.

The body of the first sacral segment is almost entirely destroyed by a large central excavation which is continuous dorsally with a similar excavation in the left ala, but which has not yet reached the auricular surface (Fig. 12). The anterior inferior extremity of the latter is invaded upon by a superficial oval excavation about 2 x 1 x 0.5 cm. The superior surface of the right ala also looks as though it had been affected. There is a good deal of deposit on the anterior surface of the second upper sacral segment, but no signs of fracture are present. The right inferior half of the body of the

second and the adjacent portion of the body of the third segments, including the intervening transverse process, are destroyed.



FIG. 12.—Sacrum with beginning of synostosed right ilium indicated, one-third natural size.

RIGHT RIBS. The first rib is completely divided in the region of the tubercle, over an area about 1×0.5 cm., on the superior surface near the dorsal margin and on the inferior surface opposite the sulcus subclavii. In the latter area the compacta contains numerous small pits, some of which are placed opposite others on the inferior surface, thus forming small canals. This portion of the rib looks worm-eaten, and again as though the disease had penetrated from without.

The fourth rib contains two tumors, about 0.75 cm. and 1.25 cm. in size, located near the middle and about 4 cm. apart. The largest of these tumors has completely destroyed the shaft and the smaller, more distant one, has almost done so.

In the fifth rib there is a defect about 0.5 cm. in size and 5 cm. medial to the angle of the rib. It is located near the dorsal border and has almost penetrated the compacta on the external surface. The compacta within is completely destroyed at this point.

There is a worm-eaten area on the superior surface of the sixth rib near its angle. This area in the compacta is about 1 cm. in size and oval in form. Most of the pits located here perforate the compacta. There also is evidence of an old tumor, with calcification, on the shaft of this rib about 7.5 cm. from its dorsal extremity. The shaft here is partly destroyed. A third tumor, about 0.5 in size, was located within 2 cm. of the costochondral junction. This seems to be at the site of an old fracture, and there also is an old healed fracture near the middle of the shaft of this rib.

There is evidence of an old lesion, about 1.75 cm. in size, near the center of the shaft of the seventh rib. There is a rounded prominence on both surfaces formed by calcifications.

The shaft of the eighth rib, in the region between the head and the tubercle—that is, the neck—is almost completely destroyed. There also was a small tumor on the inferior surface of the shaft in the mammillary line.

There is a slightly prominent, rounded area of calcification about the middle of the shaft of the ninth rib.

The superior surface of the head of the eleventh rib was slightly affected.

LEFT RIBS. A portion of the shaft of the third rib, between the tubercle and the angle, is gone. The shaft of this rib is almost completely severed, for a distance of about 2.5 cm., near its midpoint.

There is an old fracture at about the midpoint of the shaft of the fourth rib.

About 1.5 cm. of the shaft of the sixth rib is completely destroyed at a point 5 cm. from the costochondral junction. The midportion of the shaft of the eighth rib is completely severed and the same is true of the lateral extremity of the medial third of the ninth rib.

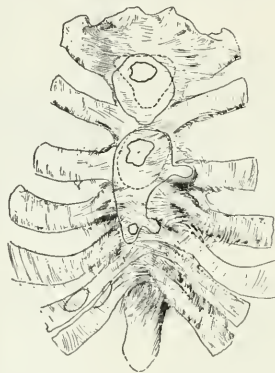


FIG. 13.—Outline drawing of the moist sternum, showing the location and size of the lesions in both bone and cartilage, one-third natural size.

STERNUM. The sternum, and some other bones was not cleaned in order to enable us to make a histological and chemical examination, if necessary, of the costal cartilages, but the size and location of the lesions is shown in Fig. 13. The caudal half of the manubrium of the sternum is occupied by a tumor which has destroyed the bone over the greater part of this area, leaving only a thin outer shell, which is still preserved on the anterior surface. Internally the tumor reaches the periosteum. Caudally it extends a little below the sternal angle, measuring approximately 3 cm. across. The second costal cartilages seem to be unaffected. The cranial portion of the corpus is completely destroyed and the third chondrosternal articulations are involved. This tumor extends down the right side of the sternum, involving also the fourth and fifth chondrosternal articulations. A marked nodular thickening is found on the third left chondrosternal articulation. At this point there is a hard, rounded prominence, 1 cm. across and 0.5 cm. high. Although the third, fourth and fifth right sternochondral articulations are also

affected, there are no prominences at these points. A small tumor is also found more caudally in the corpus. It is of particular interest, however, that the seventh right costal cartilage is affected wholly independently of an adjacent tumor. This cartilage is penetrated for about one-third of its thickness at a point about 3 cm. from the chondrosternal junction. The surface of the tumor is about 0.25 cm. large and somewhat irregular in form. The sixth right costal cartilage is also affected about 4.5 cm. from the sternochondral junction. A tumor, about 0.75 cm. across and 0.25 thick, is found on the superior surface. The muscles here as elsewhere are entirely normal and uninvaded and no changes can be seen in the perichondrium.

There also is a hard, darkened area on the superior external border of the fifth left costal cartilage. This area looks spongy, the surface being formed by a thin shell of bone, and the affected area being about 1 mm. deep, 5 mm. long and 4 mm. broad. This area is quite unlike anything else seen in this case and is probably not due to the disease.



FIG. 14.—Lateral view of the left coxal bone with the inferior portion shown separately, one-third natural size.

COXAL BONES. There are ten comparatively large defects in the left coxal bone, as shown in Figs. 7 and 14. These areas of destruction, some of which involve the entire thickness of the bone, vary from 1 to 3.5 cm. In addition to these ten areas there are two smaller ones, indicated by a question mark, which look as though the disease had just begun at these points. Had we sectioned this

bone we undoubtedly would have found indications of other lesions, but we preferred not to destroy the specimens, since the number of tumors revealed is already an exceedingly large one, and especially since the revelation of a few more small foci of disease would probably not throw any additional light upon the condition.



FIG. 15.—Medial view of the right coxal bone in bisected outline.

There are four large defects in the right coxal bone, shown in two parts, in Fig. 15. In addition to these there is a superficial defect on the external surface near the superior posterior iliac spine. This is 1 x 0.5 cm. in size, and there is another focus, 1 cm. in size, on the internal surface, making six areas of destruction in all. The size of the areas varies from 1 to 5 cm. One of the larger ones involves a portion of the acetabulum and all of the superior pubic ramus.

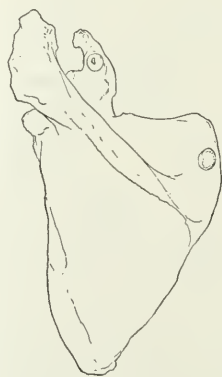


FIG. 16.—Left scapula, one-third natural size.

THE UPPER EXTREMITIES. The acromial extremity of the right clavicle is affected, especially on the surface of the distal extremity.

This area of disease was located between the cartilage and the bone. MacCallum (1901), in one of his cases, also found the end of the left clavicle distended by a tumor and the right fractured. Aside from the two tumors on the scapula and the defect in the head of the humerus, already described, no lesion was found upon examination of the fresh cleaned and cut moist specimens of the bones of the right arm. Since it was desired to use some of these bones for chemical analyses we did not clean them as we did most of the rest of the skeleton. All joints were opened, however, and the articular surfaces carefully examined. There is an area of disease, about 1 cm. in size, near the base of the coracoid process of the left scapula, and another small area near the superior angle (Fig. 16). The latter is interesting in that a fine framework of bone still remains over the entire extent of the lesion, the disease having penetrated the substance of the bone completely at many points and not completely in others.



FIG. 17.—Proximal portions of the left femur, one-third natural size.

LOWER EXTREMITIES. No evidence of the disease was found in the right leg, even upon section of the bones.

An opening about 1 cm. in size, at a midpoint, was found on the ventral surface of the left femur on a level with the caudal portion of the lesser trochanter (Fig. 17). On a sagittal section of the dry, clean bone it is seen that this opening leads into a spherical cavity in the spongiosa. The ventral compacta is also involved in the formation of this cavity, which measures 3 cm. in diameter. No other lesion was noticeable, even on section of the rest of the bones of the left lower extremity.

Although Bender (1902) stated that one cannot speak of a definite structure of the tumors in multiple myeloma, this is not true in a macroscopic sense in this case. Except for the different reactions to pressure which go with differences in size all were very much

alike. All were decidedly spongy and yielded to pressure, though firm and elastic. All tumors could very easily be removed, leaving a remarkably clean surface of wholly normal or almost normal spongiosa. The ease with which they were shelled out was largely due to the fact that the absorption of the compacta had almost kept pace with that of the spongiosa. The former formed only a small projecting margin in case of the larger tumors and was never lifted up, as in one of the cases spoken of by MacCallum (1916). There was no displacement whatever of the old compacta, the prominence in all instances being due to slight protuberance of the tumors or to calcareous or bony deposits. There was no difficulty in stripping the periosteum from the larger tumors, which included more than the majority of the S2, because of extensions into the body of the tumor. The surrounding tissues were not invaded and could always be removed without difficulty.

The surfaces of the tumors in contact with the spongiosa were fuzzy because of the extensions which had entered the cancelli before the walls had been absorbed. If any spicules of bone remained attached to these surfaces, as they probably did, they were so small that they were not noticed with the unaided eye. The edges of the bony defects were quite regular and the spongiosa showed slight sclerosis in only a few instances.

The cut surfaces of the fixed divided tumors looked grayish and the middle portion usually somewhat darker. Christian (1907, *b*) quotes Wright's autopsy notes to the effect that the tumors of his case were moderately firm, whitish and semitranslucent. Small openings, which undoubtedly were the cross-sections of bloodvessels, were fairly numerous. The bounding periosteum was always definitely delimited. While there were some gross differences the tumors were nevertheless remarkably uniform in appearance and structure.

Since the body had been preserved only in the usual routine way, and especially since the dissection was not completed until over two years after death, only a partial histological report is possible. Nevertheless, the things that remain throw some interesting side-lights on the disease.

The first thing to attract my attention was that the degenerative changes in the tumors apparently were not entirely the result of the usual postmortem changes. This, to be sure, was only an inference drawn from my experience with material from other cadavers and with other material studied, with a view of determining the degree and the order of postmortem changes in unpreserved material. Yet that the inference is probably correct seems to be indicated by several of the reports on myelomata found in the literature. This is true of the case of Bender in which portions of tumors from the vertebra, as judged by the illustrations, seem particularly degenerate. Bender also stated that the osteoclasts

and other cells showed signs of degeneration. Some of the cells in one of the photographs accompanying Wright's (1900) article also suggest that degeneration was present in them, and the same is true of some illustrations given by Hoffmann (1904) of his case. There are cells in all these illustrations which look as if they were dead or dying.

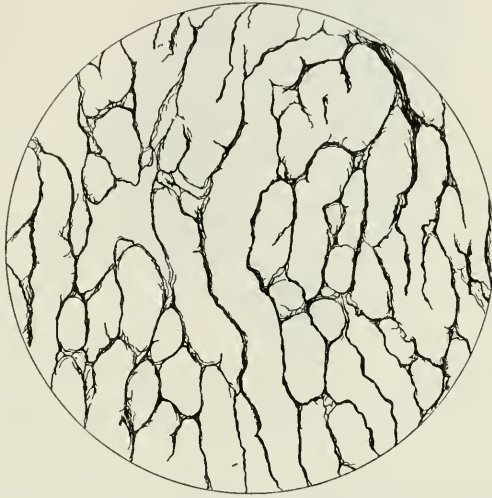


FIG. 18.—Appearance of the finer stroma. Magnification, 375.



FIG. 19.—Appearance of the denser stroma. Magnification, 375.

The stroma varied greatly in different portions of some tumors, as shown in Figs. 18 and 19. In some small areas only the very

finest, wide-meshed reticulum was present, the meshes of which were completely filled and obscured by closely packed degenerated cells. Hemorrhagic areas were present in some of them, and in



FIG. 20.—A group of cells from the better preserved portion of one of the tumors. Magnification, 750.

these the erythrocytes were quite well preserved and not infrequently completely filled the meshes of the stroma. The par-

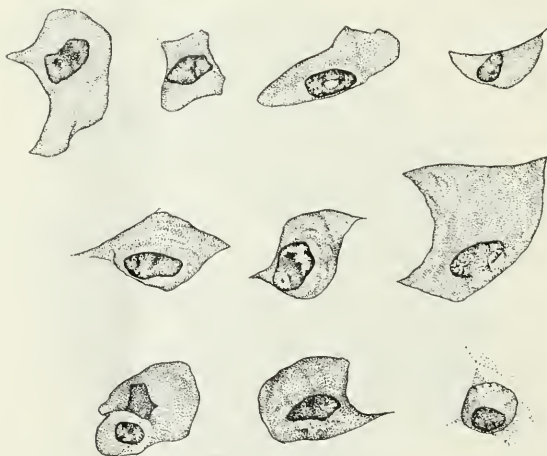


FIG. 21.—Selected well-preserved tumor cells. Magnification, 750.

enchyma also varied in different portions of the tumors, and it is evident from the close proximity of the remaining nuclei that the prevailing type of cell in some areas was not specially large. Their

size suggested lymphoid rather than myeloid cells. Fig. 20 is an oil-immersion drawing of one of the better preserved portions containing larger cells. Here the cells, although ill-preserved, are larger and quite like those shown in the illustrations of various investigators. In Fig. 21 a group of selected, quite well-preserved cells are represented under high magnification. Although these cells remind one more of myelocytes it would be idle to try to draw any conclusion from this material as to their origin.

The most interesting thing in the histological picture was the appearance presented at the line of contact between the tumor and the bone. Some of the trabeculae of the spongiosa merely looked gnawed off, presenting a ragged surface, with numerous excavations, which looked quite comparable to Howship's lacunae. Menne (1906) also mentions a many-notched appearance of the bony margins in places. In many instances these excavations were completely empty, but in others they were bordered by a row or rows of cells of the size of osteoblasts. The entire absence of osteoclasts, except an isolated specimen here or there, was very evident. The absence of osteoclasts was emphasized also by Borst, who stated that myeloplaxes are usually absent in multiple myelomata. Bender also found osteoclasts very rare in a case of multiple myeloma but exceedingly numerous in a case of lymphosarcoma. Bender accounted for the fewness of osteoclasts in myeloma by assuming that they degenerate or are formed into marrow cells, and mentions the fact that many multinucleated cells were present in Wieland's case, in which they were supposed to have been derived from the tumor cells. Menne also found osteoclasts frequently present in the lacunae, as did Abrikossoff (1903), but Adami (1910) states that in pure cases there is no overgrowth of myeloplaxes. It is not at all improbable that the differences noted in regard to the osteoclasts and also in other respects are partly due to the fact that, as emphasized by several investigators, various different things are still included under the term myeloma. Then, too, it is not unlikely that age may not be wholly without influence, although the disease is one of maturity. This is especially likely in regard to the presence of a protective reaction on the part of the bones. This might well be less in such an old individual as the present case.

The good healing of all the fractures stands in marked contrast to the slight reaction at the site of the tumors and the little callus present at the place of fractures. It is difficult also to see why so little sclerosis is evident in the spongiosa in contact with the tumor itself, especially when, as is evidently the case, the process of bone destruction is a very gradual one. That this absorption is due to pressure alone, as suggested by Bender, hardly seems probable for various reasons, but particularly because several of the lesions in this case show quite conclusively that the disease may also attack a bone from without. Then, too, if pressure were the only factor

one should not expect such symmetrically shaped tumors and defects, for the resistance of the bone surely is not uniform in all directions. This is especially true when the compacta is reached. Yet even when it is reached the defect still remains quite symmetrical in form and the progress of absorption progresses about equally in all directions.

If my interpretation of several superficial defects on the compacta is correct then it would seem to follow that the disease is metastatic, at least so far as the skeleton is concerned, or that the osteoblasts may become or give rise to tumor cells.

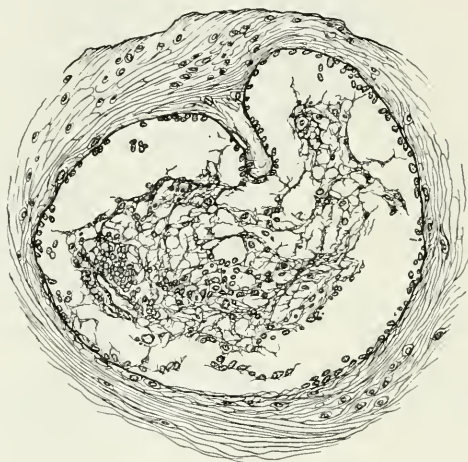


FIG. 22.—An enlarged Haversian canal lined by a layer of osteoblast-like cells. Magnification, 215.

That the process of absorption is not limited to the external surfaces of the bony area, which is directly involved, is suggested by such appearances as that shown in Fig. 22. Abrikossoff (1903) also spoke of areas which made him think of haliteresis, areas in which there was a “decalcification of the trabeculae of the spongiosa and metaplasia of the latter into connective tissue.” Bombhard, on the other hand, spoke of occasionally noticing a reaction around the tumor forming an osteoid zone. Fig. 22 shows a much-enlarged Haversian canal which contains some marrow and which is lined with a layer of cells which remind one of osteoblasts. Bender also spoke of cells lying in rows and extending into the bone. Although osteoclasts are nowhere to be seen, one can scarcely doubt that the bone absorption has been considerable here. The regularly disposed cells might also include bone corpuscles liberated by the absorption. As shown in Fig. 22 the bone corpuscles seem to be particularly numerous—in fact, increased in numbers—in some areas in the surrounding bone. In some places on the external

surface of the affected bone these cells lie in some depth, as shown in Fig. 23, where osteoclasts are again absent. In Fig. 24 a portion

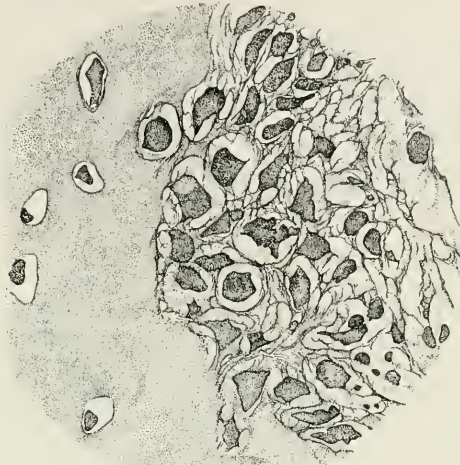


FIG. 23.—A portion of the margin of a bony trabeculum undergoing absorption. Magnification, 410.

of a trabeculum is shown at a point where it is being divided by the activity of the tumor cells. The opposed surfaces of the attached



FIG. 24.—A similar region at a place where a trabeculum is being divided. Magnification, 410.

bone look fringed and the same kind of cells are again seen both within the margins and about the bone.

These appearances as well as the character of the interior of the tumors seem to suggest that the interior of the latter is largely inert. The line of action seems to be at the periphery, but only at that portion which comes into contact with bone. The absorptive agent seems to be incapable of resorbing cartilage or periosteum.

The condition of myeloma is of special interest in the light it throws on the function of osteoclasts in bone absorption. Here we certainly have a very active absorption—in fact, a process which un doubtedly is malignant even if non-metastatic to other tissues than bone, occurring practically wholly without the intervention of osteoclasts.

A fibroid structure was revealed extremely well in some areas in the neighborhood of the tumors in the costal cartilages. These areas suggested a fibrillary nature of the cartilage as maintained by several investigators rather than the formation of new osteoid areas.

A number of samples of bone and other tissues were taken for analysis, the results of which are shown in the following tabular statement. These were dried to constant weight at 100° C., and the bone samples were extracted with anhydrous ether to remove fat. Weighed portions were then ignited in platinum dishes at low redness to constant weight, yielding data from which the loss on ignition, reported as organic matter and ash, were determined. Calcium was estimated by the method of McCrudden. Phosphoric acid was precipitated as ammonium phosphomolybdate, which was filtered off, dissolved in acid, precipitated with magnesia mixture and finally estimated gravimetrically as magnesium pyrophosphate:

The following samples were analyzed:

- No. 221. Ribs, clear sections, not adjacent to tumors.
- No. 223. Ribs, tumor-containing sections, with tumors removed.
- No. 224. Ribs, tumor-containing sections, tumors not removed.
- No. 227. Skull, tumor-containing sections, tumors removed.
- No. 226. Radius, section of bone not adjacent to tumors.
- No. 230. Tumors from rib sample No. 223.
- No. 231. Tumors from skull sample No. 227.
- No. 222. Great pectoral muscle.
- No. 220. Right biceps.
- No. 225. Parietal pleura, calcified area.

CHEMICAL COMPOSITION OF SELECTED SPECIMENS.

No.	Sample.	Organic matter, per cent.	Ash, per cent.	CaO, per cent.	CaO per cent. of ash.	P ₂ O ₅ , per cent.	P ₂ O ₅ per cent. of ash.
221 . .	Ribs	37.85	62.15	32.74	52.68	24.41	39.27
223 . .	Ribs	45.86	54.14	28.78	53.15	20.92	38.64
224 . .	Ribs	51.85	48.15	25.75	53.48	18.85	39.15
227 . .	Skull	32.79	67.21	35.75	53.19	25.53	37.98
226 . .	Radius	36.36	63.64	34.11	53.60	24.51	38.51
230 . .	Tumors	89.81	10.19	3.95	38.76	3.27	32.09
231 . .	Tumors	89.37	10.63	3.72	35.00	3.29	30.95
222 . .	Muscle	97.64	2.36	0.70	29.66		
220 . .	Muscle	98.38	1.62	0.61	37.65		
225 . .	Pleura	64.87	35.13	17.01	48.67		

Hoppe-Seyler² first called attention to a fairly constant relation between the calcium and the phosphoric acid content of bone which did not show considerable variations even when the proportion of other substances varied materially. This proportion was near to that in which these are present in the mineral apatite, the formula of which is $\text{CaCO}_3 \cdot 3\text{Ca}_3(\text{PO}_4)_2$. Levy³ has found that this relation is maintained fairly closely in osteomalacia, his analytical results ranging from 527 to 574 parts PO_4 to 400 parts of Ca instead of a theoretical ratio of 570 to 400. The above bone samples give the following values on this basis:

Number.	Sample.	Ca.	PO_4 .	10Ca : 6 PO_4 (400 : 570)
221	Ribs	23.40	32.66	400:558
223	Ribs	20.56	28.00	400:544
224	Ribs	18.40	25.22	400:548
227	Skull	25.53	34.16	400:535
226	Radius	24.39	32.79	400:537

These figures show a somewhat higher value for calcium and a lower value for phosphoric acid than the average figure for the normal human adult organism, but the difference is not great enough to have any particular significance. The percentage of inorganic constituents in all samples is low. The percentages of organic matter and ash show abnormal variations, with very low figures for the ash content, especially in the tumored rib sections.

Attention should be called to the very high percentage of calcium in the calcified area of the parietal pleura as well as to the very large amount in the muscle samples.

REFERENCES.

- Abrikosoff, A. J. (1903) Ueber einen Fall von multiplen Myelom mit diffuser Verbreitung im Knochenmark, *Virchows Arch.*, Bd. clxxiii.
- Adami, J. George (1910): *The Principles of Pathology*, Philadelphia and New York, vol. i.
- Bender (1902): Ueber ein periostales Rundzellensarcom in ein Myelom mit Kalkmetastasen, *Deutsch. Ztschr. f. Chir.*, Bd. lxxiii.
- Blatherwick, N. R. (1916): Calcium and Bence-Jones Protein Excretion in Multiple Myeloma, *AM. JOUR. MED. SC.*, N. S., vol. cli.
- Bombhard, Hans von (1914): Ein Beitrag zum Myelom, *Ztschr. f. klin. Med.*, Bd. lxxx.
- Borst, Max (1902): *Die Lehre von den Geschwulsten*, Wiesbaden, Bd. i.
- Christian, Henry A. (1907): (a) A Multiple Myeloma, *Jour. Exp. Med.*, vol. ix.
- Christian, Henry A. (1907): (b) Multiple Myeloma. An Histological Comparison of Six Cases, *Tr. Assn. Am. Phys.*, Philadelphia.
- Harbitz, F. (1910): Trophoneurotic Changes of the Bones and Joints in Leprosy, *Arch. Int. Med.*, Chicago, vol. vi.
- Hoffmann, Rudolf (1904): Ueber das Myelom mit besonderer Berücksichtigung des malignen Plasmons, *Beitr. f. path. Anat.*, Bd. xxxv.
- Lubarsch, O. (1906): Zur Myelomfrage, *Virchows Arch.*, Bd. lxxxiv.
- MacCallum, W. G. (1901): A Case of Multiple Myeloma, *Jour. Exp. Med.*, vol. vi.

² *Arch. f. path. Anat.*, 1862, xxiv, 13. *Lehrbuch der physiol. Chem.*, 1877, 104.

³ *Ztschr. f. physiol. Chem.*, 1894, xix, 238-270.

- MacCallum, W. G. (1915): A Case of Multiple Myeloma, Proc. New York Path. Soc., N. S., vol. xv.
- MacCallum, W. G. (1916): Text-book of Pathology, Philadelphia.
- Matiri, A. (1915): La malattia di Kahler-Bozzolo, con illustrazione di un nuovo caso, Policlinico, Rome, tome xxii.
- Menne, Ed. (1906): Zur Kenntniss der Myelomzellen, Virchows Arch., Bd. clxxxiii.
- Von Verebely, T. (1906): Ueber das Myelom, Beiträge zur klin. Chir., Bd. xlviii.
- Wright, J. H. (1900): A Case of Multiple Myeloma, Johns Hopkins Hospital Reports.

MENINGITIS IN THE NEWBORN AND IN EARLY INFANCY.

By MOSES BARRON, M.D.,

MINNEAPOLIS, MINNESOTA.

INTRODUCTION. Although meningitis is a disease quite common in childhood, it is one that is exceedingly rare during the early months of infancy. In making a rather careful review of the literature, I have been able to find only 39 cases reported in infants under three months old. Of these 39 cases, 19, including the case to be reported in this paper, were in the newborn.

The etiology in these cases was interesting, especially in the newborn. Of the 19 cases in this series, 7 were caused by the same type of bacillus which was isolated in pure culture from the present case, the *Bacillus coli*; 6 cases were caused by the staphylococcus and streptococcus. The infection of most of these was through a spina bifida, a condition present in nearly every one of this group. Two were caused by the pneumococcus and one each by meningococcus, *Bacillus mucosus capsulatus*, *Bacillus lactis aërogenes* and *Bacillus pyocyaneus*.

The relatively frequent occurrence of colimeningitis among the newborn is emphasized by Allard,¹ who states that this is the commonest form encountered. He believes that infants and children are specially predisposed to meningeal diseases. Moll² claims that colimeningitis in nurslings is generally consequent to colicystitis. This statement is not substantiated by a careful study of the literature. Indeed, it is definitely stated in several cases that examination of the urine showed nothing abnormal and that the specimens were sterile.

Holt³ reviews a series of 300 of his own cases of meningitis in infants up to three years old. The *Bacillus tuberculosis* was responsible for 70 per cent. of this series, but only 1 per cent. was in infants under three months old. He shows by statistics from the city of New York and from his own practice that if epidemic meningitis

¹ Die Lumbalpunktion. Ergebnisse der inneren Medizin und Kinderheilk., 1909, Bd. iii, S. 100.

² Prager med. Wchnschr., 1907.

³ Observations on 300 Cases of Acute Meningitis in Infants and Young Children, Am. Jour. Dis. of Child., 1911, i, 26.

be excluded, from 55 per cent. to 70 per cent. of all cases of meningitis in infants and young children are tuberculous in origin. Practically no cases of colimeningitis are reported in children over six months old. Smith⁴ states that 75 per cent. of all cases of tuberculous meningitis in children occur before the fifth year. The largest number occur during the second year. He also mentions the fact that, exclusive of epidemic meningitis, 70 per cent. of all meningeal infections are tuberculous. These statistics, together with the tables to follow, help to emphasize through contrast the variations in susceptibility of infants of different age periods to the various infecting agents.

REVIEW OF THE LITERATURE. The earliest cases of meningitis which I found in the literature were reported by Sherer (1895⁵). He reported 3 cases in infants from eight days to six weeks old. One of these cases was a weak, jaundiced infant nine days old, suffering from vomiting, diarrhea and rapid loss in weight. It died, with definite meningeal symptoms, nine days later. At the autopsy considerable pus was found covering the convexity and the base of the brain. A bilateral suppurative otitis media was present. The bacteriological report was colimeningitis. Two other cases of infants, eight days and six weeks old respectively, occurred in the same hospital during a period of a little over a year. All presented the same type of lesions: fibrinopurulent colimeningitis and bilateral otitis media. Sherer considers his 3 cases as a small epidemic, due to overcrowding in the hospital. He thinks that the infection originated through the contaminated water used in bathing the infants. The infected material, lodging in the external ear, started the otitis media. From this location the infection spread to the brain. It is also possible for the infection to have gained entrance through the mouth and from there to have been carried through the lymphatics or, more probably, through the Eustachian tubes to the middle ears and then to the brain.

Hinsdale(1899⁶) describes a case of meningitis in an infant, three days old, caused by *Bacillus coli immobile*. The mother had suffered with an acute metritis following a miscarriage two years previously. During and after the expulsion of the placenta, large quantities of pus escaped from the uterus. The infant began losing in weight and on the third day the emaciation was quite marked. Nystagmus and retraction of the head were present from birth. Convulsions appeared on the fourth day. The umbilical cord had a fetid odor. The infant would not nurse and died on the thirteenth day. At autopsy an abscess was present in the left frontal lobe of the brain

⁴ Meningitis in Infancy, Illinois Med. Jour., 1913, No. 3, xxiii, 299.

⁵ Ein Beitrag zur Aetologie der Leptomeningitis Purulenta bei Säuglingen, Jahrbuch f. Kinderheilk., 1895, Bd. xxxix, S. 1.

⁶ Purulent Encephalitis and Cerebral Abscess in the Newborn Due to Infection from the Umbilicus, AM. JOUR. MED. SC., 1899, cxviii, 280.

in addition to the exudate on the surface. There was an induration of the abdominal wall around the navel. The infection in this case probably arose from the previous endometritis. The process extended through the placenta to the fetus.

Scheib(1900⁷) cites a case of an eight-day-old infant who died with the diagnosis of general debility. At autopsy a purulent meningitis was found, caused by the *Bacillus lactis aërogenes*. This organism is considered a frequent cause of meningitis in infancy, but this case is the only one I found recorded.

Goldreich(1902⁸) cites an interesting case of antenatal infection with *Bacillus coli*. Convulsions, together with cyanosis, jaundice, diarrhea, rigidity of neck and irregular respirations, appeared in the infant on the first day of its life. It died on the second day. The principal finding at autopsy was a fibrinopurulent meningitis. A purulent pleuritis and acute bronchitis were also present. It is hardly conceivable that the infection in this case did not happen until after birth. The author suggests that the bacteria might have gained entrance into the uterus during labor, which in this case lasted three days. On the second day the amniotic sac ruptured, opening an avenue for the entrance of germs. Then the fetus aspirated some of the contaminated fluid through premature respirations. From the lungs the infection was carried to the brain by the blood. Such a presumption helps to explain the bronchitis and pleuritis as well as the meningitis found at autopsy. This is probably the youngest case of suppurative meningitis reported in the literature.

Benfey (1907⁹) cites a case of *Bacillus pyocyaneus* meningitis for the purpose of proving the pathogenicity of this organism. He reports a case of a seven-day-old infant who developed meningeal symptoms and died on the eighth day. The navel was distinctly inflamed and the author believes that it was the portal of infection. At autopsy a pure culture of *Bacillus pyocyaneus* was recovered both from the purulent exudate on the brain and from the blood.

Noeggerath's case (1907¹⁰) was in a female infant, sixteen days old, who was well up to the eleventh day. She then developed abdominal cramps and symptoms of meningitis. A purulent exudate was present on the umbilicus. In the eighth week a double otitis media appeared. An organism was isolated which seemed to correspond to *Bacillus coli*, but had properties also of *Bacillus lactis aërogenes*. It was encapsulated and quite motile. It was identified as *Bacillus coli immobilis capsulatus*. Stern¹¹ and Conradi and

⁷ Prager medicin. Wehnschr., 1900, S. 169.

⁸ Meningitis beim Neugeborenen, Jahrbuch f. Kinderheilk., 1902, Bd. lvi, S. 808.

⁹ Ueber Pyozyaneussepsis, Med. Klinik, 1907, Nr. 40, S. 1199.

¹⁰ *Bacillus Coli Immobilis Capsulatus* bei Einem Falle von Eitriger Meningitis Cerebrospinalis, München. med. Wehnschr., 1907, Nr. 13, Bd. liv, S. 617.

¹¹ Zur Kenntnis der Pathogenen Wirkung des Koli beim Menschen, Deutsch. med. Wehnschr., 1893.

Bierast¹² speak of the many variations that may occur in the *Bacillus coli* when it becomes pathogenic. Noeggerath thought that the infection in this case was either through the navel or through the intestinal tract. An argument against the navel route was the microscopic finding of the umbilical vessels, which showed no evidences of any inflammation.

Holt (1911¹³) reports a series of 300 cases of meningitis in children under three years old, but from the data given I could classify only 11 of them as occurring in infants under three months old. Of these 11, 3 cases (a very large percentage) were due to *Bacillus tuberculosis*; 6 cases to staphylococcus and streptococcus and only 1 case to *Bacillus coli*. The last case presented meningeal symptoms only. It became sick when four weeks old and died in the sixth week. A pure growth of *Bacillus coli* was obtained from the purulent fluid removed from the spinal canal. The author cites an additional case of colimeningitis from his private practice. This was in a four-weeks-old infant who had previously suffered from a colon infection of the urinary tract.

Pearson's case (1912¹⁴) was in a female infant, three months old. At autopsy the *Bacillus coli communis* was isolated from the spinal fluid and from the purulent exudate enveloping the brain and filling the ventricles. There was also an acute suppurative otitis media present. The author holds this latter condition responsible for the meningitis.

Smith and Woodforde (1912¹⁵) report a case of colimeningitis in an infant somewhat older than the usual incidence of this infection. Their patient was five months old. The organisms isolated were very motile. The disease at first responded to autogenous vaccine therapy, but later the patient died. The urine in this case was sterile. The authors consider the meningitis as a primary infection.

A case of meningitis caused by the *Bacillus mucosus capsulatus* is reported by Bonhoff and Esch (1912¹⁶). The infant was born in asphyxia. A catheter was inserted into its trachea to initiate respiration. Small quantities of amniotic fluid and mucus escaped from the mouth when the infant started breathing. The first four days it was restless, whimpered a great deal and did not nurse well. Clonic contractions appeared in the face muscles and in the back muscles on the sixth day. The development of emaciation was rapid. Spinal fluid was removed and examined but no cultures were made. Death occurred on the fourteenth day. At autopsy

¹² Kolle-Wassermann: Handbuch der Pathogenen Mikroorganismen, 2 Auflage, Bd. vi, S. 483.

¹³ Loc. cit.

¹⁴ A Case of Meningitis in Which the *Bacillus Coli Communis* was Obtained from the Cerebrospinal Fluid, *Lancet*, London, 1912, clxxxii, 722.

¹⁵ Two Unusual Forms of Meningitis Occurring in Infancy, *Lancet*, London, 1913, clxxxiii, 236.

¹⁶ Ueber Einem Fall von Meningitis purulenta beim Neugeborenen, infolge rechtseitiger Mittelohrentzündung, *Ztschr. f. Geburtsh. u. Gynäk.*, 1912, Bd. lxx, S. 886.

there was pus present over the brain and in the right middle and internal ear. Culture from the pus on the brain and from the middle ear showed a pure growth of Friedländer's bacillus.

Lyall (1913¹⁷) gives a detailed report of a case of typhoid meningitis in a female infant four months old. She died six weeks after the onset of the symptoms. The postmortem examination showed a diffuse purulent meningitis with no lesions present characteristic of typhoid fever. The author thinks that the infection in this case took place through the intestinal tract.

Giese (1913¹⁸) reports the only case of influenzal meningitis in a young infant found in the literature, though some authors state that this type of infection is not uncommon.

Von Reus (1914¹⁹) reports a case of coliform meningitis in a newborn infant. The case is cited by Michael,²⁰ with no data given.

Hermann (1915²¹) reports what he considers the only case of pneumococcic meningitis in the newborn. When thirteen days old the infant was taken sick. It died at the age of seventeen days. No meningeal symptoms were present at any time, yet the autopsy revealed a purulent meningitis as the only lesion present. Culture of the pus gave a pure growth of pneumococci. The author discusses the possible portals of infection. The umbilical route he considers rare. Premature respiration of the infant during difficult labor, he believes, may result in the aspiration of contaminated liquor amnii and thus start the infection. Infection may also occur through an injury to the skull during delivery. After birth the mouth, nose, throat, *intestinal tract*, ears, eyes, umbilicus or urinary tract may be the portals of entry. He states that the contaminated water of the bath-tub is a frequent source of infection, and thus agrees with Noeggerath²² and Sherer.²³

Michael (1916²⁴) recovered the *Bacillus coli communis* from the spinal fluid of a five-months-old infant. It died two weeks later. The organism was very motile. The exudate was described as a thick brownish pus, a characteristic mentioned by a number of authors.

A valuable contribution to meningitis in infants is made by Koplik (1916²⁵). He reports, with some detail, his findings in 12 of his own cases. Four of his cases were due to streptococcus; 3 to

¹⁷ Meningitis in an Infant Caused by the Typhoid Bacillus, Jour. Med. Res., 1913, No. 4, xxvii, 457.

¹⁸ Ugeskrift for Laeger, Copenhagen, 1913, No. 16 (Abs. in Jour. Am. Med. Assn.).

¹⁹ Cited by Michael (20).

²⁰ Recovery of the Colon Bacillus from the Spinal Fluid of a Five-months-old Infant, Arch. of Ped., 1916, xxxiii, 280.

²¹ Meningitis in the Newborn, with Report of a Case, Arch. of Ped., 1915, No. 8, xxxii, 583.

²² Loc. cit.

²³ Loc. cit.

²⁴ Loc. cit.

²⁵ Meningitis of the Newborn and in Infants under Three Months of Age, Arch. of Ped., 1916, xxxiii, 481.

pneumococcus; 4 to meningococcus; 1 to *Bacillus coli*. One case of the streptococcus, 1 of the meningococcus and the case of *Bacillus coli* meningitis showed symptoms within a few days after birth.

Case No.	Author.	Year.	Age.	Type of bacterium.	Probable portal of entry.
1	Sherer	1895	Newborn	<i>B. coli</i>	Otitis media.
2	Sherer	1895	Newborn	<i>B. coli</i>	Otitis media.
3	Sherer	1895	6 weeks	<i>B. coli</i>	Otitis media.
4	Hinsdale	1899	Newborn	<i>B. coli</i>	Placenta.
5	Scheib	1900	Newborn	<i>B. lactis aërogenes</i>	
6	Goldreich	1902	Newborn	<i>B. coli</i>	Lungs.
7	Benfey	1907	Newborn	<i>B. pyocyaneus</i>	Umbilicus.
8	Noeggerath	1907	16 days	<i>B. coli</i>	Intestinal.
9	Holt	1911	3 months	<i>B. tuberculosis</i>	
10	Holt	1911	3 months	<i>B. tuberculosis</i>	
11	Holt	1911	3 months	<i>B. tuberculosis</i>	
12	Holt	1911	Newborn	Staphylococcus and streptococcus	Spina bifida.
13	Holt	1911	Newborn	Staphylococcus and streptococcus	Spina bifida.
14	Holt	1911	Newborn	Staphylococcus and streptococcus	Spina bifida.
15	Holt	1911	Newborn	Staphylococcus and streptococcus	Spina bifida.
16	Holt	1911	Newborn	Staphylococcus and streptococcus	
17	Holt	1911	Newborn	Staphylococcus and streptococcus	
18	Holt	1911	4 weeks	<i>B. coli</i>	
19	Holt	1911	4 weeks	<i>B. coli</i>	
20	Pearson	1912	3 months	<i>B. coli</i>	Suppurative otitis media.
21	Smith and Woodforde	1912	5 months	<i>B. coli</i>	Hematogenous.
22	Bonhoff and Esch	1912	Newborn	<i>B. mucosus capsulatus</i>	Eustachian tube.
23	Lyll	1913	4 months	<i>B. typhosus</i>	Intestinal.
24	Giese	1913	?	<i>B. influenzae</i>	
25	v. Reus	1914	Newborn	<i>B. coli</i>	Hematogenous.
26	Herrman	1915	Newborn	Pneumococcus	
27	Michael	1916	5 months	<i>B. coli</i>	Hematogenous.
28	Koplik	1916	Newborn	Meningococcus	
29	Koplik	1916	6 weeks	Meningococcus	
30	Koplik	1916	3 months	Meningococcus	
31	Koplik	1916	3 months	Meningococcus	
32	Koplik	1916	Newborn	<i>B. coli</i>	Circumcision.
33	Koplik	1916	6 weeks	Streptococcus	
34	Koplik	1916	7 weeks	Streptococcus	
35	Koplik	1916	3 months	Streptococcus	
36	Koplik	1916	6 weeks	Streptococcus	
37	Koplik	1916	Newborn	Pneumococcus	
38	Koplik	1916	8 weeks	Pneumococcus	
39	Koplik	1916	3 months	Pneumococcus	
40	White	1917	29 days	Meningococcus	
41	White	1917	39 days	Catarrhalis (?)	
42	Barron	1917	Newborn	<i>B. coli</i>	Mouth (?)

The above table gives in tabulated form all the cases within the ages under discussion which were found in the literature.

The last-mentioned case occurred in a male infant who was circumcised on the eighth day. Three days later a colipyelitis set in, which was followed a week afterward by colimeningitis. The patient died at the age of sixteen months from asthenia and necrosis of both eyes, associated with marked hydrocephalus. The author emphasizes the fact that infections may occur through abrasions in the buccal mucous membranes produced by the accoucheur.

White (1917²⁶) reports 2 cases in infants twenty-nine and thirty-nine days old respectively. The meningitis in the first case was caused by the meningococcus. From the second case an organism was isolated which was thought to be the *Micrococcus catarrhalis*. However, this diagnosis is questionable.

The following table gives the classification of the above forty-two cases according to ages:

Newborn	19
Two weeks to one month	4
One month to two months	7
Two months to three months	8
Three months to five months	3
Exact age uncertain	1
	<hr/>
Total	42

Subtracting the 3 cases of three to five months old leaves 39 cases under three months.

The following table shows the classification of the 19 newborn cases according to etiology:

<i>Bacillus coli</i>	7
<i>Streptococcus</i> and <i>staphylococcus</i>	6
<i>Pneumococcus</i>	2
<i>Meningococcus</i>	1
<i>Bacillus mucosus capsulatus</i>	1
<i>Bacillus lactis aërogenes</i>	1
<i>Bacillus pyocyaneus</i>	1
	<hr/>
Total	19

The following table shows the classification of the 42 cases according to etiology:

<i>Bacillus coli</i>	14
<i>Streptococcus</i> and <i>staphylococcus</i>	10
<i>Meningococcus</i>	5
<i>Pneumococcus</i>	4
Tuberculosis	3
<i>Bacillus mucosus capsulatus</i>	1
<i>Bacillus influenzae</i>	1
<i>Bacillus typhosus</i>	1
<i>Bacillus lactis aërogenes</i>	1
<i>Bacillus pyocyaneus</i>	1
<i>Bacillus catarrhalis</i> (?)	1
	<hr/>
Total	42

²⁶ Case Reports of Infectious Meningitis Occurring in Babies Twenty-nine and Thirty-nine Days Old Respectively, Arch. of Ped., 1917, xxxiv, 372.

The above shows that the *Bacillus coli* causes practically 33 per cent. of all cases of meningitis in infants under three months. (Three cases in the table are over three months old.) Of this 33 per cent. (14 cases), one-half (7 cases) occurred in the newborn. This is strongly in contrast with the etiology of non-epidemic meningitis in infants of the second year of life, as is well brought out by the statistics of Holt²⁷ and others.

CASE REPORT.—My own case is that of a male infant, eleven days old, who was delivered in breech presentation. The mother is a hard-working woman, aged forty-four years, who has had eight pregnancies, including the last one. Six children are living and well. During the latter months of the last pregnancy the mother experienced pain in the epigastrium which was of the character of real labor pains during the last two weeks before delivery. She noticed that her abdomen was excessively enlarged. The childbirth, she thinks, was about one month premature. The confinement was in the home, with practically no medical attention up to the second stage of labor. That there was a condition of hydramnios became evident when, during the second stage of labor, more than 1 gallon of amniotic fluid escaped. The delivery of the head was assisted by the insertion of a finger into the mouth of the fetus and then using a moderate amount of traction. The infant was cyanotic at birth, and it required considerable effort to initiate respiration.

The infant had a whimpering cry and at no time nursed well. A slight right-sided paralysis made its appearance on the third day. The right hand appeared puffy and edematous. On the tenth day there was a bilateral swelling of the eyelids. Several slight convulsions were noticed on the morning of the eleventh day. The lips turned cyanotic. The child died on the same day.

Autopsy Protocol. I performed the autopsy fourteen hours post-mortem. I shall indicate only the important findings.

The body is fairly well developed, somewhat undernourished. The skin and conjunctivæ are slightly jaundiced. There is a depression 3 mm. deep over the left parietal eminence. This measures 2 x 4 cm. The skin over it is not abraded. The umbilicus has dropped off; the navel is dry and appears healthy. The right lung shows petechial hemorrhages beneath the pleura and in other portions of the parenchyma. The gastro-intestinal tract shows no lesions and appears entirely normal. Both adrenals are large, distended and of a bluish-red color. On section, large hemorrhages are found involving the medullæ, which extend more than half the distance into the cortices.

In removing the scalp no lesions are visible over the depressed area, nor is there any evidence of injury to the brain after the calvarium and dura mater are removed. The brain is found covered with a layer of brownish fibrinopurulent exudate. This is most

²⁷ Loc. cit.

marked over the left parietal region. The base of the skull and middle ears are free from lesions.

Smears from the exudate show disintegrated pus cells and immense numbers of extra- and intracellular Gram-negative, short, plump bacilli.

Microscopically the lungs show small areas of congestion and hemorrhage. The heart and spleen are normal. The liver shows a mild fatty metamorphosis. Many of the cells are swollen and their nuclei are vesicular. The adrenals show hemorrhages into the medullæ, with only an occasional parenchymal cell visible. The inner portions of the cortices are torn; the cords of cortical cells are separated by areas of hemorrhage. The kidneys show intense congestion of the glomerular tufts. The thymus shows moderate "accidental" involution.

The brain parenchyma is normal. The pial vessels are greatly dilated. The arachnoid space is filled with an exudate of fibrin, a few red blood cells and masses of leukocytes, nearly all of which are polymorphonuclears. In some areas the exudate consists almost wholly of fibrin and red blood cells.

Bacteriological Studies. Cultures were made from the exudate and from the heart's blood. This, together with the animal inoculations, was performed by Dr. Arthur T. Henrici. I am indebted to him for the data of the bacteriological studies.

The report states that the smears from the pus show a very short, Gram-negative coccobacillus. Some of the bacilli stain more deeply at the poles than in the middle and give the appearance of diplococci.

The cultures from the heart's blood showed no growth. The first cultures from the pus showed a short, slender bacillus, with a few coccoid and irregular forms. Some forms possessed club-shaped extremities. The subcultures and all subsequent cultures gave a fairly uniform bacillus typical of *Bacillus coli*. In hanging-drop preparations all of the cultures showed a very active, typhoid-like motility.

The cultural characteristics of this organism on the different media are as follows:

Agar: spreading, moist, grayish growth.

Broth: uniform turbidity.

Gelatin stab: filiform growth; no liquefaction.

Litmus milk: first culture acid in four days; no coagulation.

Subsequent cultures: acid in two days; coagulation in seven days; very little whey expressed.

Peptone solution: indol in four days.

Sugars: dextrose, acid and gas in twenty-four hours.

maltose, acid and gas in twenty-four hours.

mannite, acid and gas in twenty-four hours.

lactose, acid in forty-eight hours; gas in four days.

saccharose, no acid and no gas.

(Gas formula = $\frac{\text{CO}_2}{\text{H}_2} = \frac{1}{2}$.)

In all the subcultures the lactose fermented a day or two later than did the other sugars.

From the above it will be seen that the organism recovered was definitely the *Bacillus coli communis*, but the marked motility and the tardiness in its action on lactose at first suggested the *Bacillus paratyphosus*.

Inoculations into rabbits and guinea-pigs, either intravenous or intraperitoneal, killed the animals in from twelve to forty-eight hours. The organism was recovered from the blood in each case. No immunity reactions were performed.

COMMENT. Conradi and Bierast²⁸ speak of the variations in size, shape and motility in *Bacillus coli*. They also mention that some strains are slow in fermenting lactose. Actual mutations are thought to occur, and these strains are sometimes designated as *Bact. coli mutabile*. Most of the strains of *Bacillus coli* isolated from the meningitis cases here reported were actively motile.

The susceptibility of infants to *Bacillus coli* infections has long been noted. Beitzke²⁹ states that *Bacillus coli* is the principal causative agent of pyelitis, pyelocystitis and pyelonephritis. It also sometimes produces intestinal diseases, general sepsis and meningitis. Yet in the adult this organism is almost entirely a saprophyte, being a constant inhabitant of the intestinal tract, and rarely does it become pathogenic. But since the protective powers of the infant are very feeble the bacillus occasionally gets a foothold and becomes pathogenic. Halban and Landsteiner state that infants possess a very low capacity for the manufacture of protective substances. Artificially-fed infants are said to be even more susceptible to infections than breast-fed ones, because the mother's milk contains immune bodies which are utilized by the infant.

La Fetra³⁰ does not believe that infants are born septic very often. Such instances, he thinks, are indeed rare. He also doubts that infection is common through the aspiration of contaminated liquor amnii, as claimed by Sherer³¹ and others. Bonhoff and Esch,³² on the other hand, claim that in their case the infection was through the Eustachian tube, brought about by the aspiration of liquor amnii during premature breathing in intra-uterine life. The fluid and mucus which escaped from the mouth of the infant at the beginning of respiration certainly warrants such a contention. The introduction of the catheter may also have carried the infection. Aschoff³³ has found in his careful studies that the passage of liquor amnii up the Eustachian tubes during premature respiration is fairly common. He, however, believes that the inflammation resulting from

²⁸ *Loc. cit.*

²⁹ In Bruning und Schwalbe's *Handbuch der Allgemeine Pathologie*, Bd. i, S. 252.

³⁰ *Accidents and Diseases of Early Weeks*, *Arch. of Ped.*, 1916, xxxiii, 401.

³¹ *Loc. cit.*

³² *Loc. cit.*

³³ *Ztschr. f. Ohrenheilk.*, Bd. xxxi, S. 295.

it is not due to infection introduced but only to the fluid itself acting as a foreign body. Rasch³⁴ studied the postmortem findings relative to middle-ear diseases in 82 autopsies on infants up to two years old. He found that fully 75 per cent. had either unilateral or bilateral middle-ear involvement, many cases of which were purulent in character. Several cases had meningitis associated with it. Such a finding strongly suggests that meningitis must be not infrequently secondary to middle-ear infections. If this finding be correlated with the finding of Aschoff,³⁵ that there is a *locus minoris resistentie* in the middle ears due to the presence of aspirated amniotic fluid, then the sequence of events leading up to many cases of meningitis becomes almost self-evident.

But La Fetra³⁶ believes that the umbilicus is the most important route. Also that the skin and mucous membranes are frequent avenues because these tissues are comparatively undeveloped at birth. The intestinal mucous membrane, for example, is undoubtedly pervious to bacterial invasion without any evident lesions. The cases of bovine tuberculosis in infants and young children without intestinal tuberculosis certainly corroborate such a concept. As to the mucous membrane of the mouth, as a portal of entry, one can get little definite proof. In my case I believe that the infection occurred through the introduction of the accoucheur's finger during delivery. Koplik³⁷ calls attention to this method of introducing infection. A woman who has not been properly prepared for delivery will have the vulva more or less contaminated with fecal material. The introduction of a finger into the mouth of the infant in the process of delivery might create just the proper conditions for infection: the introduction of the infectious agent and the abrasion of the covering epithelium, the mucous membrane.

There is some evidence in favor of the idea that the external auditory canal is also an important avenue for infection in the infant. Rasch³⁸ believes that of the two avenues of infection of the middle ear, that of the Eustachian tube and of the external auditory canal, the latter is the more important one.

GENERAL CONCLUSIONS. 1. Meningitis in the newborn and in early infancy is a rare disease.

2. The important place that the *Bacillus tuberculosis* holds in the meningitis of later infancy the *Bacillus coli* occupies in the early months of infant life.

3. Pathogenic strains of *Bacillus coli* may show marked variations in form, in rates of fermentation and in motility.

4. The avenues of infection of the newborn have not been definitely established. Nevertheless, infection through the mouth

³⁴ Ueber die Häufigkeit und Bedeutung von Mittelohrentzünd bei Kleinen Kranken Kindern, Jahrbuch f. Kinderheilk., 1894, Bd. xxxvii, S. 319.

³⁵ Loc. cit.

³⁶ Loc. cit.

³⁷ Loc. cit.

³⁸ Loc. cit.

by means of fingers or instruments of the accoucheur must always be borne in mind and proper precautions taken accordingly.

5. It is reasonable to believe that some infections occur in the bath-tub through water that has become contaminated. The portals of entry of the bacteria may be either through the external auditory canals, the mucous membrane of the mouth, the Eustachian tubes or the intestinal tract.

6. The susceptibility of infants to infection with organisms, that are otherwise only slightly pathogenic, may be explained by the feebleness of antibody production during the early months of infancy. The greater resistance of breast-fed infants over the artificially-fed ones is probably due to the compensation of the passive immunization by the breast milk for the active immunization which is still deficient.

THE PROGNOSIS OF EXOPHTHALMIC GOITRE.

BY E. MACD. STANTON, M.D., F.A.C.S.,

SCHENECTADY, NEW YORK.

SEVEN years ago I read before the Schenectady County Medical Society a paper on the surgical treatment of goitre. The discussion which followed was confined largely to the question of exophthalmic goitre; it was a typical discussion such as usually follows whenever the subject of exophthalmic goitre is brought before a general medical society.

An analysis of the facts brought out in this discussion showed that every man taking part reported at least one case cured or satisfactorily improved under some form of treatment, but that no two men had used the same form of treatment and no one man had used the same form of treatment in more than one cured case.

From the facts brought out in this discussion we can draw the following conclusions:

1. A certain proportion of exophthalmic goitre cases recovered under such diverse forms of treatment that we must come inevitably to the conclusion that the disease is self-limited in some as yet not definitely determined proportion of cases.

2. Before really definite opinions can be expressed concerning the value of any particular form of treatment we must have a fairly definite conception of the life history of the disease. We must know what ultimately becomes of patients undergoing various forms of treatment or no treatment at all. The results of the various methods must be compared, and it must be determined whether or not they show results differing from those to be ordinarily expected in the natural course of the disease.

3. The fluctuations in the course of the disease as regards individual cases during short periods of time is so variable as to make conclusions based on individual or small groups of cases followed for a short period of time almost of no value whatever.

Following the above-mentioned discussion I determined to collect from the literature as much as possible of the available published data concerning the prognosis of exophthalmic goitre. This data I analyzed in two ways: (1) as regards the general conclusions arrived at by the many writers on this subject, and (2) by taking the actual case results as reported by the individual writers and reanalyzing their data in so far as it had a bearing on the questions under consideration.

For this latter part of the work a standard form, such as is used in census and actuarial investigations, was devised, showing the total number of cases of each author available for the purposes of our study, the number treated by excision, ligation, or sympathectomy, Beebe serum or simple medicinal means and the period during which the patients had been followed as under one year, from one to three years, three to five years or over, five years and the final condition—cured or satisfactorily improved, somewhat improved, not improved or dead.

Could one tabulate a sufficient amount of accurate data in this way it would be possible to chart an average or composite picture of the life history of the disease under each particular form of treatment. The accurate available data was, however, only sufficient for one to gain a general impression as to what these curves would be if we had had sufficient data to plot the complete curves.

From the literature then (1913) available my assistant, Dr. Deeds, and I were able to collect reports of end-results based on a total of 2880 cases, and eliminating duplicates when two or more writers have made use of the same clinical material, we had left 1623 cases divided as follows:

Excision of one lobe, 610

Sympathectomy, 231

Serum, 442

Medical, 330.

All of the older and much of the recent data is complicated by including as exophthalmic goitres cases exhibiting symptoms of goitre toxemia as a complication of large non-hyperplastic goitres, the so-called aplastic-toxic cases of the Mayo classification. My remarks concerning exophthalmic goitre are intended to apply to the true hyperplastic cases presenting the typical symptoms-complex of Graves's or Basedow's disease.

Basing my conclusions largely on the above-mentioned data, I believe that we can state, with reasonable certainty, that typical exophthalmic goitre of the Basedow type is in a majority of cases a

self-limited disease. Plummer, of the Mayo Clinic, states that the height of the intoxication is usually recorded during the first year. Toward the close of the second year I believe that we may expect about one-third of the cases to have so far recovered as to be able to continue at their normal occupations, while at still later periods others improve so that we may count on 60 to 70 per cent. of spontaneous recoveries after a period of five or six years. These conclusions agree with those of Hale White, who was able to trace 87 exophthalmic goitre patients who had been treated in Guy's Hospital and in his own private practice, and after a number of years found 61 of these patients cured and 21 decidedly improved, leaving only 5 of the 87 unimproved.

The medically treated cases studied by us showed a mortality of approximately 10 per cent. during the period they were under observation. Hale White found 15 deaths among 102 exophthalmic goitre patients. He compared the actual deaths with the expected deaths in healthy insured individuals of the same age for the same period of time and found the mortality among the exophthalmic cases to be only twice that of the normal death-rate for healthy persons of the same age as determined by life-insurance experience. This is not a high mortality, and in life-insurance work is equalled by many occupations and conditions not ordinarily considered to be specially dangerous.

My studies of the prognosis of exophthalmic goitre have led me very firmly to the belief that there are only two major factors in the non-operative treatment of exophthalmic goitre—namely, rest and time. Drugs and various other measures may tend to give some degrees of temporary subjective relief, but there is no proof in any of the articles so far published that the improvement noted is anything other than that to be expected in the natural course of the disease.

With the above somewhat sketchy outline of the normal prognosis of this disease it is evident that the surgeon must accomplish certain very definite results if he is to prove that surgery is to have a permanent place in the treatment of exophthalmic goitre.

At the very lowest estimate from 20,000 to 30,000 operations have been performed in this country during the past ten years for exophthalmic goitre, and yet, except for some fragmentary data as to the operative mortality and the general trend of the end-results as obtained in several clinics where very special skill has been developed in handling these cases, the medical profession is in almost complete ignorance as to the actual results obtained through this very large number of operations for exophthalmic goitre.

Similar lack of adequate end-result knowledge could be cited in many other fields of surgery. Several reasons have been assigned for this lack of knowledge, such as the difficulty of keeping track of patients and the time and labor required to ascertain and record

the results. My own end-result studies, carried out over a period of ten years, have convinced me that these excuses are mere details and that the chief reason for our present-day lack of end-result knowledge is that surgeons have not as yet devised a uniform and satisfactory system for reporting the data which they have been able to collect. Surgical literature is full of communications dealing in a general way with the subject of end-results, in which it is evident that the author is in possession of considerable data which he has finally despaired of presenting in other than the most general terms.

Some time ago I found that I had several thousand histories with end-result records extending over fairly adequate periods of time, but that whereas these records had been collected with, let us say, one unit of energy on my part, when I came to study any one group of cases it took several units of time and energy to put the data into form suitable for study and comparison. In some groups it was impossible to classify the results according to the usually attempted standards. Also, I found that no two surgeons adopted the same standards in reporting their cases, so that it was impossible to compare small groups from different sources or to combine them into larger series of greater statistical value.

The real reason for this difficulty lies in the fact that surgeons have tried to state the end-results in terms such as "cure," "improved," etc., without reference to the time element. Actually, our patients are cured, or whatever the result may be, for variable periods of time, and it is just as absurd to try to state end-results in terms ignoring the element of time as it would be to attempt to state the area of a plot of ground in terms of one dimension.

All of the major difficulties of presenting the end-results disappear if we tabulate the results in terms of the time the patients have been traced following the operation, together with their state of health for the time periods. By this method the "cured" column becomes "years cured," and the term "years" is also added to the other divisions. It is also of advantage to add the headings "years operated" and "years traced," as illustrated in the accompanying table, which shows the results of tabulating 26 exophthalmic goitre cases operated by myself.

The mortality may be recorded either as "years dead" or by simply giving the number of deaths. In the cases here reported the operative and late deaths are given in separate columns, also the expected mortality in normal individuals for the same period is indicated.

The advantages of this system of recording end-results are quite obvious. No matter how complicated the postoperative history, it can be readily subdivided and classified into the appropriate periods.

RESULTS FOLLOWING OPERATIONS FOR EXOPHTHALMIC GOITRE.

Case No.	Years op.	Years traced.	Years cured.	Years satisfactorily improved.	Years improved.	Years unimproved.	Deaths.	
							Immediate.	Late.
2	10	3	3			
3	10	10	8	1	1
4	9 ¹ / ₁₂	8 ¹⁰ / ₁₂	7 ⁴ / ₁₂	1 ⁶ / ₁₂				
5	8 ¹¹ / ₁₂	8 ⁶ / ₁₂	6 ¹¹ / ₁₂	⁶ / ₁₂	1		
6	8 ¹⁰ / ₁₂	8 ¹⁰ / ₁₂	7 ¹⁰ / ₁₂	1			
7	8 ⁶ / ₁₂	8 ² / ₁₂	6 ² / ₁₂	2				
8	7 ¹¹ / ₁₂	7 ³ / ₁₂	6 ⁹ / ₁₂	⁶ / ₁₂				
9	7 ⁸ / ₁₂	1	⁶ / ₁₂	⁶ / ₁₂		
12	6 ⁸ / ₁₂	6 ⁸ / ₁₂	5	1 ⁸ / ₁₂				
13	6 ⁶ / ₁₂	5 ⁹ / ₁₂	5 ¹ / ₁₂	⁸ / ₁₂				
16	5 ¹⁰ / ₁₂	⁹ / ₁₂	⁹ / ₁₂				
18	5 ⁸ / ₁₂	4 ⁹ / ₁₂	1	
19	5 ⁶ / ₁₂	5 ⁶ / ₁₂	1 ⁶ / ₁₂	4			
21	5 ⁴ / ₁₂	5 ⁴ / ₁₂	4 ⁴ / ₁₂	1				
28	4 ⁶ / ₁₂	3 ⁷ / ₁₂				
30	3 ⁹ / ₁₂	2 ⁵ / ₁₂	2 ⁶ / ₁₂	1	
32	3 ⁶ / ₁₂	3 ⁶ / ₁₂	2 ⁶ / ₁₂	⁶ / ₁₂	1
33	3 ⁶ / ₁₂	3 ⁴ / ₁₂	3 ⁴ / ₁₂				
40	2 ⁵ / ₁₂	1 ⁶ / ₁₂	1 ⁸ / ₁₂			
41	2 ³ / ₁₂	1 ¹¹ / ₁₂	1	
42	2 ² / ₁₂	1	1				
43	1 ⁹ / ₁₂	1 ⁶ / ₁₂	¹¹ / ₁₂	⁶ / ₁₂			
44	1 ⁹ / ₁₂	1 ⁷ / ₁₂	1 ³ / ₁₂	⁴ / ₁₂			
45	1 ⁸ / ₁₂	1 ² / ₁₂	1 ¹ / ₁₂	¹ / ₁₂			
47	1 ⁶ / ₁₂	1	⁶ / ₁₂	⁶ / ₁₂				
49	1	1	⁹ / ₁₂	³ / ₁₂				
Total	136 ⁶ / ₁₂	107 ⁷ / ₁₂	50 ⁸ / ₁₂	20 ⁵ / ₁₂	22 ³ / ₁₂	2 ⁶ / ₁₂	3	2 ¹

It is not necessary for the surgeon to trace each case to the time of reporting his results. If he has lost track of his patient soon after operation this fact is clearly shown by his figures and the value of the data may be judged accordingly.

Formerly the most difficult of all cases to classify were the exophthalmic goitre cases. This was because almost no single case could be placed under a single heading. By the method here outlined even the exophthalmic goitre cases can be readily classified. The table shows 26 cases operated, a total of $136\frac{5}{12}$ years and traced $107\frac{7}{12}$ years. Of this time $50\frac{6}{12}$ years, or 47 per cent., of the total traced postoperative time the patients have been cured. An additional $20\frac{5}{12}$ years, or 9 per cent., of the time the patients have been satisfactorily improved, making 66 per cent. of truly satisfactory results. $22\frac{3}{12}$ years, or 21 per cent., credited in the improved column, represent improvement to such an extent that the patients feel well repaid for their operations. Only $2\frac{6}{12}$ years, or 2 per cent. of the postoperative time, has been passed as unimproved.

¹ The expected mortality for healthy individuals of the average age of these patients traced for an equal length of time would be 0.963, or approximately 1.

In my series there were 3 early postoperative and 2 late deaths. The expected mortality for normal risks of the average age of the patients in this series is 0.963, or not quite 1 normally expected death.

I believe that much of the time credited to the improved column in the table could properly be listed under the satisfactorily improved column. Thus Case II was practically cured of all symptoms of hyperthyroidism, but before and after operation she also suffered from true hysteria. In Case III the microscopic examination of the thyroid tissues removed was reported as probably malignant, being a solid, hugely cellular tumor. This patient was able to resume her normal occupations and continued in fair health for eight years, after which time she had a slow-growing malignant recurrence, from which she died nine years after the operation. I know of no other case on record of a patient living nine years after an operation for a malignant tumor of the thyroid. Case XXX reported as only improved, and yet he passed the physical examination for the Italian army and was killed in action on the Austro-Italian front in 1916.

It is worthy of note that 97 per cent. of the cured time is assigned to patients operated more than five years ago, while the more recent cases are found listed in the improved columns.

An analysis of the individual cases shows that in each patient a marked improvement followed almost immediately after the operation. In the majority of cases this improvement continued progressively, so that after from six months to two years the patient could be classed as cured. In every case the immediate improvement in the subjective symptoms was very marked. This was often out of proportion to the demonstrable improvement in the pulse, tremor and exophthalmos.

The improvement in the pulse rate and tremor was, however, always demonstrable at an early date. Most patients gained from 15 to 30 pounds in weight within a few months of the operation. As a rule, the exophthalmos disappears slowly, and for a long time following the operation the pulse rate is markedly increased by exertion or excitement.

Temporary acute recurrences of toxic symptoms are frequently met with during the first year or more following operation. These usually subside in a few weeks or they may be controlled by hot-water injections into the remaining gland tissue.

CONCLUSIONS. Removal of a portion of the thyroid gland of patients suffering from exophthalmic goitre produces a profound immediate effect noticeable within a few days of the operation and characterized chiefly by an improvement in the subjective symptoms of discomfort felt by the patient, but also accompanied by a marked fall in the pulse rate, a diminution of the tremor and an increase in weight.

This initial improvement, however, seldom amounts to a cure. The exophthalmos usually persists for months or years. The heart remains irritable, the pulse becoming rapid with exertion or excitement and at irregular periods we may expect acute exacerbations of toxic symptoms, which may alarm both the patient and the surgeon.

The general tendency is, however, toward improvement rather than recurrence, and after a variable length of time a few patients may have failed to improve or even have grown worse; but the great majority, I believe about 80 per cent., will have continued to improve, so that finally practically all traces of their former trouble disappears.

It is useless for the surgeon to claim that there is no medical side to the treatment of exophthalmic goitre. After five or six years there is probably little to choose from between the medical and surgical end-results as regards either the mortality or the condition of the surviving patients.

Patients surviving operation have been promptly relieved of the more distressing subjective symptoms, and the majority of them will have been able to return to their normal work in about half the time that it would have taken them to reach the same state of improvement under medical treatment. Against this is the primary mortality which must always accompany operations for exophthalmic goitre unless we are to deny the chance of operative relief to many cases most in need of the relief.

In the future the man best able to treat exophthalmic goitre will be the one who has developed the judgment necessary to enable him to select the treatment, medical or surgical, best adapted to the individual case. The decision will depend upon many factors, not the least of which will have to do with the social condition of the patient, and whether she or he can afford the time and expense necessary for the prolonged rest required to effect a medical cure.

THE CLINICAL DISPLAY OF SYPHILIS OF THE NERVOUS SYSTEM.¹

BY JOSEPH COLLINS, M.D.,

PHYSICIAN TO THE NEUROLOGICAL INSTITUTE OF NEW YORK.

THERE is no other way of convincing ourselves and our colleagues that syphilis attacks and disorders the nervous system early and often than to keep repeating it and furnishing new proof. Such repetition would seem trite and platitudinous did not our daily experience convince us that many patients with syphilitic disease

¹ Read before the American Neurological Association.

of the nervous system are neither correctly diagnosed nor properly treated until the disease has existed so long that it is practically incurable. Until it is generally recognized (1) that syphilis is the most common cause of all organic nervous disease; (2) that the treponema invade the nervous system soon after the general infection; (3) that there are certain physical signs which are the hall-marks of syphilis of the nervous system; (4) that proper laboratory study of the serum and cerebrospinal fluid in conjunction with examination of the patient will make the diagnosis in every instance. I feel it my duty to continue to call attention to the frequency of syphilitic disease of the central nervous system and to the fact that it displays itself often as a clinical imposter.

FREQUENCY OF SYPHILITIC DISEASE OF THE NERVOUS SYSTEM.

During the past seven and half years there have been examined in the first division of the neurological institute, 12,468 patients. A considerable number of them, just how many I am not at this time prepared to say, suffered from metabolic disorders and from intoxications and infections other than syphilis. The diagnosis of syphilis of the nervous system was made or suspected 2036 times, *i. e.*, in about one-sixth of the cases. During the same period 3840 new patients were admitted to my service in the wards of the hospital, and of this number 922, practically 25 per cent. were found to be suffering from disease of the nervous system that had its origin in syphilis. Of these 922 patients I have taken the records of 830 which are sufficiently complete to satisfy the requirements of this inquiry and attempted to make a clinical diagnosis of each one of them. The result is set forth in the accompanying table:

Meningitis (basilar 19, cortical 13)	32
Meningo-encephalitis	5
Apoplexy	28
Progressive hemiplegia	7
Encephalitis (pseudoparesis)	6
Brain tumor	7
Epilepsy	8
General paresis	140
Imbecility (dementia)	4
Acute mania	5
Melancholia	7
Paranoid state	2
Korsakow's syndrome	1
Headache	16
Migraine	8
Insomnia	7
Neurasthenia	17
Thalamic syndrome	4
Weber syndrome	2
Pontobulbar	5
Bulbar apoplexy	3
Cerebellar syndrome	3
Ponto-medullo-cerebellar space	1
Dysarthria	1
Disseminated sclerosis	4

In this connection it may be said that I have for some time dispensed with making a clinical diagnosis of syphilis of the nervous system in all cases save tabes and general paresis. The etiological diagnosis, and usually the anatomical diagnosis, is made.

The most striking facts that these statistics set forth are: (1) syphilis of the nervous system constitutes about 25 per cent. of the neurologist's work; (2) tabes and general paresis constitute about one-half of syphilis of the nervous system; (3) when syphilis invades the nervous system the symptoms that result resemble so closely those of any disease of the nervous system that expert examination is necessary to detect it. The third of these statements requires some discussion, though it may be considered an elaboration of the obvious. In the table there are a certain number of cases of migraine, of trigeminal neuralgia, of poliomyelitis, of arthritis deformans, etc. I am not attempting to prove that there is such a disease as syphilitic migraine or syphilitic poliomyelitis. An individual who has had syphilis and upon whose soma it has written its signature may have attacks of migraine, of trigeminal neuralgia, of poliomyelitis or any other disease without such disease being of syphilitic nature. When the physician attempts the interpretation of such a case he must decide for himself whether or not the disease which the patient then has is of syphilitic origin. My criteria are if there is no other attributable cause, and if the disease yields to antispecific treatment, I am suspicious that the disease is of syphilitic origin. When I discover alteration in the cerebrospinal fluid, which is satisfactory evidence of an active syphilis in the central nervous system, my conjecture becomes a certainty. For instance, a patient who recovers from trifacial neuralgia under vigorous salvarsan and mercurial medication and whose serum and cerebrospinal fluid (Wassermann) becomes negative is considered by me to be a case of luetic tic douloureux.

INTRACRANIAL SYPHILITIC DISEASES. There is nothing particularly noteworthy about the meningeal diseases due to syphilis in these statistics, save the fact that it did not seem justifiable to make the diagnosis of pachymeningitis, but in one instance, and that the basilar form of meningitis, was not, as it has usually been stated to be, so much more frequent than the cortical. The explanation of this is, I think, that the diagnosis of meningeal involvement was often made largely from a study of the cerebrospinal fluid in individuals who complained of headache, dizziness, malaise and prostration. Unless there was evidence of involvement of the cranial nerves the designation "basilar" was not added to the diagnosis "meningitis." That there is involvement of the meninges in many cases of cerebrospinal lues is beyond question, and when examples of such infection come to autopsy extensive characteristic lesions are found. Nevertheless, syphilitic disease of the coverings of the brain causing characteristic symptoms of meningitis is rather

unusual. The point that I desire to make is that syphilitic disease of the cerebral meninges often does not cause the ordinary clinical manifestations of meningitis.

The diagnosis of meningo-encephalitis was made when the individual had objective manifestations of syphilis plus symptoms of irritation of the meninges and of the cortex which has special functional allotment.

For instance an umbrella polisher complained for a week or so that the right hand and arm got tired easily. Then he developed headache which in a few days was followed by a right-sided facial paralysis. Examination four days later showed right seventh nerve paralysis of the peripheral type, right brachial monoplegia, partial astereognosis and lively tendon-jerks of the right upper and lower extremities, serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin plus, Fehling's plus and cells 85. Within a week he had a typical Babinski big toe phenomenon of the right side, but no indication of hemiplegia. He recovered and the serology became negative.

The most likely diagnosis in such a case would seem to be meningo-encephalitis of the lower left Rolandic cortex. The laboratory reports conclusively exclude a vascular lesion, and a peripheral lesion would not be adequate to explain all of the manifestations.

The relationship of disease of the cerebral bloodvessels to syphilis is a definite one, and the facts of it are firmly established clinically and anatomically.

There is nothing particularly new brought out by study of our cases of cerebral apoplexy, save the fact that in some of them were it not for the existence of a positive serum reaction the arterial disease would not be attributed to syphilis. For instance, a brewery worker, aged forty-nine years, who denied having had syphilis, awakened at 3 A.M. with cramp in the left leg. On attempting to move the leg with the left hand he found he could not. The left hand felt as if it were asleep. He walked about for an hour or so then the symptoms disappeared. At 9 A.M. the left side became paralyzed. The leg recovered in two days, but the upper extremity was quite paralytic when he was examined five days later. In addition there was partial left lower facial palsy, the tendon jerks of the lower extremity were exaggerated and the Babinski big toe phenomenon was elicitable. Superficial and deep sensibility were normal and the pupils were circular and responded to light. The serum Wassermann was plus, cerebrospinal fluid negative throughout, systolic blood-pressure 180. Without the laboratory findings the case would have been considered an arteriosclerotic cerebral thrombosis, but with them we must assume it to be one of luetic arteritis. No one would think of denying that a patient with symptoms of aortitis whose blood serum showed a positive Wassermann was suffering from vascular syphilis.

The cases of progressive hemiplegia in our series, 7 in number, were of a fairly constant clinical type which bespoke their dependency upon luetic endarteritis.

Syphilis of the brain displays itself occasionally in such a way as to suggest a diagnosis of brain tumor. But these statistics do not seem to show that gumma of the brain is often diagnosed as brain tumor. Often the symptoms yield with astonishing readiness to appropriate treatment. A married Italian, aged thirty-seven years, who became infected with syphilis when he was thirty-three, complained in August that his right side felt queer, especially the arm. About six weeks later, while cutting a piece of ice, the right hand began to jerk and the right side of the face screwed up. This disappeared in a short time. He did not lose consciousness and he did not become paralyzed. Later he complained of severe headache. Three months later he had another attack, in which he became partially hemiplegic and unable to talk, and with this there developed left strabismus. On March 1, 1917, his complaint was of severe headache, dizziness, vertigo, diplopia, inability to talk understandingly, poor memory and right-sided hemiplegia.

Examination showed evidence of slight right-sided hemiplegia, left external rectus palsy and 3 diopters of papilledema.

Laboratory examination: serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, cells 22, globulin plus, Fehling's plus.

May 1, 1917, all subjective and objective symptoms, save occasional vertigo, had disappeared.

Epilepsy occurring in an individual who has had syphilis is presumed to be luetic. It need scarcely be said that an individual with idiopathic epilepsy may contract syphilis which shall have no relationship to his nervous disease. Syphilitic epilepsy is the expression, as a rule, of a focal encephalitis or meningo-encephalitis, chiefly vascular or of a gumma which does not produce characteristic manifestations of increased intracranial pressure.

Epilepsy as the result of luetic infection may be expected to give one or more of the reactions found with a positive serology. Of this the commonest is a positive serum Wassermann and the rarest a general paresis colloidal gold curve. The latter, however, will occur in a parietic with epileptiform manifestations. There are many disorders or diseases classified under the name epilepsy that give a positive Wassermann reaction, the result of a luetic focus outside of the nervous system; but there are cases of epilepsy that give a positive Wassermann reaction in a peculiar fashion not the result of syphilis. At present it must be interpreted as an idiosyncrasy of the particular patient. These reactions are characterized by a negative Wassermann reaction in the serum when cholesterinized antigen is used and a strongly positive reaction when the non-reinforced extract is used. This paradoxical behavior which has yet to be explained is found only in some patients, about 30 per cent. of our own cases.

WHAT IS PSEUDO GENERAL PARESIS? If there is such a disease as pseudoparesis it is a disease founded on disseminated encephalitis.

Pseudoparesis is a very indefinite designation. What most writers mean to convey by it is that the individual who has the disease resembles a paretic, but that some of the cardinal features are lacking. The course of the disease does not conform to that of general paresis and sometimes it terminates in recovery. I have had the experience which I have no doubt many others have had, to be obliged to transfer cases labelled pseudoparesis into the category of true paresis after an interval of several years. On the other hand, I have had the experience to do the reverse. I am suspicious of the correctness of my diagnosis of pseudoparesis until after a number of years has elapsed. There is no doubt that syphilis of the brain causes occasionally mental and emotional disorder suggesting general paresis, but some one of the essential features of the disease is lacking. It is particularly in these cases that the laboratory is of signal aid in making a diagnosis.

The paretic curve of the colloidal gold reaction has been demonstrated to be a most trustworthy diagnostic criterion. Many cases which are not typical of general paresis may unhesitatingly be diagnosed when this test is positive.

For instance, take the case of a barber, aged twenty-eight years, who maintained that he was well until February 28, 1914, when he slipped on the icy sidewalk, and in attempting to save himself from falling wrenched his body. The next morning he was unable to walk properly because of numbness of the right side, which increased for forty-eight hours and practically incapacitated him. It then gradually grew less, but the right side of the body always remained weak, and it was for that weakness that he sought relief. Physical examination showed arterial hypertonus, systolic blood-pressure of 250; weakness of the right extremities as compared with the left, with livelier tendon-jerks, Babinski and ankle-clonus on the right side, and Argyll-Robertson pupils. Mental examination showed impaired memory, poor attention, fair insight and slight depression. There were no delusions and nothing suggestive of seriously impaired judgment. He made some mistakes in writing and in computation, and when they were pointed out to him he contended that he was no scholar. Laboratory examination: serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin plus, cells 190, Fehling's plus, colloidal gold, typical paretic curve. This patient died in a State hospital two years after the beginning of the disease and the diagnosis was general paresis.

In contrast with this case was one in which suspicions of general paresis had been entertained. A railway engineer, aged sixty-three years, was seen October 26, 1910. Three months before that date he began to experience a sensation of dizziness, especially when he stooped or made the least effort. Soon after this he got

generally weak, so that at times he was unable to reverse the lever of the locomotive, and often had to ask his fireman to do it. He then developed within a few weeks headache, especially in the left temple, drowsiness, crying spells without cause, inability to speak clearly—that is, to say what he wanted to say—disturbance of articulation, forgetfulness, disordered vision and loss of weight. Physical examination showed a blood-pressure of 140, and a sphygmographic tracing revealed a moderate degree of peripheral obstruction; tremor of the outstretched fingers and of the lips and indistinct articulation. Mental examination revealed depression, impaired memory, defective attention, loss of insight and poor judgment. Emotionally he was very unstable. Laboratory examination: serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin negative, cells 11, Fehling's plus. He received two treatments of salvarsan and protracted mercurial treatment. A letter from him seven years later, recently received, states that he is perfectly well and that he has been steadily at work as a locomotive engineer since six months after his stay in the hospital.

As a matter of fact neither of these cases is an example of pseudoparesis in the sense that I use it. The term "pseudoparesis" I apply to a form of cerebrospinal syphilis which is anatomically found chiefly in endarteritis, the lesions being very diffuse and not chiefly of the cortex, but of the basilar ganglia, the latter being responsible for the bilateral physical symptoms which they almost always display. One of the best examples of that disease is a young man, now in the Manhattan State Hospital, who came under my observation two and a half years ago. He was then thirty years old. He became infected with syphilis when twenty-four and had been under treatment off and on since that time; mercury internally and by inunctions and three intravenous injections of salvarsan. Early in January, 1915, he began to complain of headache, loss of memory, frequent dizziness, drowsiness and disinclination to work. It was noticed by his family that his speech had become slow and laborious, that he was slow of comprehension, that his handwriting was unsteady, while his employer had noticed that he made mistakes in his clerical work. Within a fortnight his condition became very much worse. On January 14 it was noted that there was a slight left-sided paralysis, though he could walk without evidence of hemiplegia, and he could also use his left hand. The next day he was mildly delusional, thought his dead father was living and believed his brother who had married and moved to his own house was still at home. He thought people had been to see him who had not been. His memory for past events was excellent but poor for current events. His discourses were intelligent, and he recognized people, pictures and objects and was able to read correctly a few newspaper headings, but could not read the paper. He was exceedingly drowsy and tended constantly to fall asleep, complained of headache, backache, pain in the left shoulder and felt very stupid.

He was admitted to the hospital on January 18, 1915. Physical examination revealed fine tremor of the lips, tongue and hands, overactive tendon-jerks, Argyll-Robertson pupils. Serological examination: serum Wassermann plus, cerebrospinal fluid plus, globulin plus cells 30, Fehling's solution plus. The colloidal gold test did not show the characteristic paretic curve of general paresis. Mentally he was well oriented, recalled when he had come to the out-patient department, gave a description of the physician who had examined him, but he was somewhat confused about dates, the month and day, and tended to fabricate mildly. He told of having written certain letters, having gone out to mail them, stopped at certain places, during which time he was in the hospital. He was not euphoric, he had insight as to his condition and he was solicitous about his welfare and recovery. On the evening of the next day the patient suddenly went into a state of collapse; breathing rapid and stertorous; body covered with cold sweat; pulse, 76; blood-pressure, 135. This was soon followed by complete right-sided hemiplegia and total aphasia. The following morning the hemiplegia was only partial and the patient coöperated well during the examination, apparently comprehending everything that was said to him and occasionally making spontaneous utterances, such as "it hurts." All the tendon-jerks were exaggerated, those of the left side livelier than the right, the left ankle displaying a typical (the right an incomplete) clonus, and the Babinski phenomenon was elicited in both feet. Ten days later the evidences of hemiplegia had practically disappeared, his physical condition remained otherwise about the same. Mentally his condition did not differ materially from that of the time of his entrance. He became very easily fatigued, and when fatigued was confused and his answers were not always responsive or intelligible. On February 6 he had another collapse attack, even more profound than the previous one. Pulse, 120; respiration, Cheyne-Stokes type; cold extremities; on this occasion there was no paralysis. A week later it was noted that the patient was again fabricating and was slightly confused. He answered questions promptly, most of them correctly, but displayed very little interest in things going on in the world or immediately about him. There was now very little trace of the right-sided hemiplegia in his gait or use of the upper extremity. His condition gradually improved, and on February 19, his serology being then negative and he having had five intravenous injections of salvarsan, he was allowed to go home. He received another salvarsan treatment in March and another on April 2. It was then noted that there was no gross disturbance of memory either for past or recent events. His behavior was orderly and he was well oriented for time and space. There were no indications of delusions or hallucinations. His answers were terse and to the point. He had good insight into his condition; regarding himself,

he was much improved, but not profoundly well. He thought, however, that he was well enough to be allowed more independence than he had, such as to go to the barber alone, etc. The pupils were irregular, and of the Argyll-Robertson type; slight right facial weakness; no tremor of the lips; the tendon jerks were all exaggerated and the ankle and Babinski phenomenon remained as before. The laboratory reports at this time were all negative, save that the cerebrospinal fluid showed an excess of globulin.

May 10 the serology was again negative. Nevertheless he was given an intravenous injection of salvarsan. His memory was good for past events and better than for recent. It was difficult for him to give details of anything. He recalled persons that he met, but was unable to recall the conversation he had with them. He had no delusions and no grandiose ideas. The grasp of a subject was poor and he admitted that he did not quite understand everything that he read or what was read to him. He knew, however, that he had a paralytic stroke; understood the nature of his disease; realized that his mind was unbalanced and he was ashamed of sexual excitement which he had had and which he recalled.

May 25 he became violently excited, profane, obscene and indulged in the most abandoned sexual conduct. A physician was called who gave him an injection of morphin. The next morning he refused to come to the hospital but was persuaded to do so, and when he arrived there he maintained that he had come to his senses. His physical and mental condition did not seem materially different from that when he was last examined. Two years after that date Dr. Hoch writes his physical condition showed bilateral increase of knee-jerks, right more than the left, bilateral Babinski, slightly slurred speech, tendency to convulsive laughter, pupils that respond sluggishly to light and negative laboratory report, save a slight increase of globulin. On the mental side it was difficult to establish a definite intellectual defect, but he seemed to be somewhat shaved off, somewhat childish and possibly did not fully appreciate his situation. He had had several intraspinal salvarsan treatments without discernible affect.

It is very interesting to contrast this case with another that we have had under observation for upward of seven years. The patient was a young man of education and social distinction, aged thirty-two years, who contracted syphilis when eighteen. It is probable that he had little or no treatment. When he was thirty-one years, he began to complain of insomnia and nervousness and felt "run down." He took a protracted holiday and then returned to his journalistic work. On or about this time he consulted Dr. James J. Putnam, complaining of pains in the lower part of the back and buttocks, constipation, stiffness of the knees and ankles, with occasional sharp pains, numbness in the feet, sensation of being unsteady while walking in the park, slow micturition, impaired

sexual potency and constipation. The pupils were normal, speech was distinct, intelligence unimpaired and tendon-jerks normal. The only objective signs were disorder of deep sensibility in the toes and feet and well-marked Romberg. The diagnosis of tabes was made. A few months later he became unconscious suddenly and remained so twenty minutes, then he went into a profound sleep and on awakening he vomited. The next day, however, he went to the office and kept at work for four months—namely, until February 9, 1909—when he became garrulous, expansive, hilarious and hallucinatory. In this hallucinatory state he had to be carefully guarded.

April 26, 1909, he had a generalized convulsion and was unconscious half an hour. A month later he had another convulsion, and after this attack it was noted that his memory was impaired. During the remainder of 1909 he had eight convulsions accompanied by loss of consciousness and followed in several instances by inability to speak for a time, varying from a minute to three days.

October 24, 1910, he had five convulsions in succession, lasting altogether about three hours, and following this status epilepticus he was unable to speak for three days. After this he displayed increased mental enfeeblement. In the latter part of December, 1910, the attacks assumed the petit mal type, and from March 20 to March 25, 1910, he had a series of these petit mal attacks, constituting a milder form of status epilepticus than in the previous October. These attacks lasted for from two to three minutes and began with manifestations of increased restlessness and excitement. He usually began yelling "Oh! oh!" and then became slightly rigid, the face suffused, the eyes twitched and he appeared to lose consciousness for a few moments. After the attack was over he was quiet, subdued and listless for a variable time. It was related when he was brought to the hospital March 29, 1910, that he had not spoken since the series of attacks four days before. Examination showed a powerfully built, well-nourished young man who displayed the following physical signs: irregular Argyll-Robertson pupils, slight ataxia of station and gait, absent knee- and ankle-jerks. He did not answer questions, though apparently able to hear. He spoke rarely if he desired something, fed himself, was interested in his appearance and clothes and in general comported himself like a rational person. He read the papers, but often gazed for a long time at one article; he played solitaire and smoked and was fairly amenable to hospital routine.

Laboratory examination: serum Wassermann plus, globulin plus, Fehling's plus, cerebrospinal fluid (Wassermann) plus, cells 13. He was put on active mercury treatment and not seen again until June 27, 1910. It was then noted that he talked if he wished something, but would not respond to questions. He would not go out with his nurse but would go out with his sister. He seemed to have

forgotten his friends when they came into the room where he was. He would stare at them but would not speak. He slept fairly well but arose early, dressed himself and was busy doing trifling things—playing with a picture puzzle, twisting a string, going through his pockets, etc. He rarely spoke when he wanted anything, but he would draw a picture of it and then take it to his sister and hold it before her gaze. He insisted upon having his own way and became excited and angry if he was resisted. In July it was noted that one night after a short nap he began to talk. He said that he had no recollection of leaving Boston or of the circumstances attending it; that he did not know how long he had been in New York and inquired what had happened. He said his head felt queer, then he got a dictionary and looked up the word "insane." He then went to his sister and patted his chest and said he was insane. He then went back to bed and the next morning when he awakened he was in his customary state of silence and purposeless activity. He had no grand mal attacks after this time but he had frequent petit mal attacks. From this time onward his voluntary speech grew gradually less, until about in a year he ceased to speak at all. Many attempts were made to test his sense of hearing, but without result. There was gradual impairment of physical and mental vitality. He had to be constantly cared for like a young obstreperous child. He was not violent unless he was crossed, and when handled the right way, particularly by his sister, he was fairly tractable. His only mental activities seemed to be in doing simple picture puzzles; his sole diversion was in smoking and aimless arranging and rearranging his things, dressing and undressing. He received much antisypilitic treatment, salvarsan and mercury, and the serological reactions all became negative. Sometimes it appeared that he was more intelligent, more tractable, more capable of looking out for himself, but each succeeding year he was more demented and more infirm physically. The early winter of 1917 a more decided change came about in him. He began to have attacks in which he would laugh, shout, *halloo* and yell at the top of his voice. These seemed to have replaced the petit mal attacks which had been so frequent in the previous year. They came in spells and lasted for a few minutes to two or three hours, and while seized with them he was very boisterous and difficult to control. It was also noted that he was not conducting himself as well as usual. When walking on the street with his sister he would attempt to stop women and shake hands with them. In eating he would stuff his mouth full of food and then attempt to take some liquid; it would run out over his clothing and the table. He lost all sense of modesty. The most striking feature of his conduct, however, was his motor restlessness. He would scarcely remain quiet for a minute unless occasionally when he was engaged in making simple picture puzzles. He would dress and undress many times a day. No sooner had he finished

dressing than he would start undressing, and *vice versa*. He would put something out of his hand like a nail file or watch and then search for it here, there and everywhere. If he did not find it he would go to his sister and by gestures and yelling make a disturbance until it was given to him. Then in a minute he would mislay it again and the search would begin all over. In the meanwhile he had become much more unsteady on his feet and his hands displayed great loss of dexterity. His general make-up was that of a very weak-minded and undisciplined child. The remarkable feature of it is that he had never become violent to such a degree that his sister could not readily soothe him. The only distinct recollections that he seemed to have were of habits, such as smoking; when a strange man came in the room the patient would point to his pocket and make gestures of smoking: a request for a cigarette. When walking in the street he would endeavor to drag his sister into a cigar store. He recognized a picture of his mother who had died during his illness and he often led his sister to it. Restlessness, sleeplessness, dementia and attacks of yelling, screaming and laughing, which seemed to have replaced the petit mal attacks, were the distinguishing features of his condition. From 1911 to 1916 his Wassermann reactions were practically negative. Laboratory report on May 1, 1917: serum Wassermann weakly plus, cerebrospinal fluid (Wassermann) plus, globulin plus, cells 12, Fehling's plus, colloidal gold, typical paretic curve.

In other words, nine years after the onset of the disease that had been considered typical parenchymatous cerebrospinal syphilis he presents the laboratory features of a general paretic and the clinical features of a terminal dement.

The larger my experience the more convinced I become that pseudo-general paresis nearly always eventuates in general paresis. The modern treatment of syphilis of the brain displaying itself in the guise of paresis delays the progress of the disease, increases the intervallary periods, during which the disease seems to be in abeyance and the patient able to resume the ordinary duties of life, shapes in an obstruction measure in many instances the course of the disease, but despite this the outcome finally is general paresis and dissolution.

SYPHILIS AND MENTAL DISORDER. The relation of syphilis to mental disorder aside from general paresis is strangely negative save for a form of subacute dementia, subsequent to and associated with a semidelirious state which terminates in more or less complete recovery.² It has small relationship to the causation of mental disorders that lead to insanity. In a few instances syphilis of the brain displays itself by symptoms which in their ensemble constitute mania, melancholia and involuntional states, but here again it

² For detailed examples see the writer's Neurological Clinic, Paul Hoeber, New York, 1918.

is difficult to decide whether or not their occurrence in syphilis is not a coincidence. Syphilis has a definite relation to mental and emotional disorder and disequanimity which does not lead to insanity. It may have a relationship to disorderly conduct and unlaudable behavior from which disease of the nervous system indirectly flows, such as the use and abuse of alcohol, intemperateness in other directions, and thus be a contributory cause of mental disease, of its rebelliousness to treatment. The possibilities of its entailments often cause depression, anxiety, agitation and sometimes obsessive states, and it may well cause that instability of the mind and emotions in the descendants, which we speak of as the psychopathic constitution. Granted all this, syphilis has a strange aloofness from all mental disorder save general paresis, considering the readiness with which it invades and conquers the central nervous system.

SYPHILITIC DISEASE OF THE MIDBRAIN AND PONS-OBLONGATA. The midbrain and pons-oblongata is a favorite location for syphilitic vascular and meningovascular disease. In 23 instances of this series the chief location of the disease was there. There is nothing particularly noteworthy about any of these cases save the typicalness of the clinical pictures and the fact that some of them had existed for a long time. The series includes one case of pontobulbar luetic disease which I published twenty years ago.³

THE LUTIC SPINAL CORD DISEASES. It seems quite incredible that a few years ago it was widely held that tabes was not a syphilitic disease, so universal is its acceptance now. The fact that it is diagnosed earlier and from fewer data than it was formerly accounts for what seems to be its greater prevalency. It constitutes about one-seventh of all nerve syphilis.

Some of the cases that I have included under the caption of myelitis others might have been placed under the heading of early tabes, but in reality there is no clinical diagnosis that can be made satisfactorily. For instance a pressman, aged thirty-nine years, who became infected with syphilis when he was twenty-eight, complained that he had difficulty in holding the urine of six months' duration and of partial impotency. On inquiry he admitted that for several years he had seen double once in a while, and at times the legs felt very heavy and tired easily. He also admitted that recently he had a sensation of numbness in the heels. Physical examination was quite negative, save that the pupils had lost their contour and that the light reaction was sluggish. His laboratory report was: serum Wassermann negative, cerebrospinal fluid positive, globulin positive, cells 61, Fehling's positive, colloidal gold, non-paretic curve. In reality the only suitable diagnosis to make in such a case is cerebrospinal syphilis.

³ Medical Record.

There are very few clinical problems that are more difficult to solve than the distinction between disseminated sclerosis and disseminated cerebrospinal lesions of syphilitic origin. As a matter of fact it has been my experience that at times the diagnosis cannot be satisfactorily made. I have in mind a patient who has been under observation for the past five years, a young man now thirty years old, and who had never had syphilis. He complained in his twenty-fourth year of difficulty in starting the urinary stream; a year later he noted that his eyesight was failing. Within a month walking became difficult, he wavered from side to side, his heels would come down first and he would have difficulty in maintaining his balance. A month later he complained of numbness and tingling in the right hand and loss of skill in using it. Six months later he complained of numbness and tingling in the feet and legs extending up to the knees and a sensation in the feet as though they were wrapped in cotton. He grew steadily worse, all save the vision, which seemed to remain stationary. Physical examination showed difficulty in standing and walking; gait spastic ataxic; no tremor; tendon-jerks exaggerated; double Babinski; abdominal and epigastric reflexes absent. Ocular examination: pupils slightly irregular in shape and size; light and convergence reaction good; no diplopia; no nystagmus; vision: right 6/200, left 5/200; for 2 mm. test object large central scotoma in each eye; peripheral field normal; fundi, slight; diffuse pallor, more marked in the temporal half of each optic nerve; arteries rather small, not sclerotic. General interpretation of ocular condition: retrobulbar neuritis with central scotoma in each eye. No marked emotional instability; no speech defect; memory good; attention excellent.

Laboratory report: serum Wassermann plus, cerebrospinal fluid negative. He received five doses of salvarsan and was not seen again for three years. Meanwhile he had been to Germany; received further salvarsan medication there and mercury treatment at one of the spas. His infirmity had progressed in every feature. He now recalled that when he was about twenty years of age he had a small preputial ulceration to which he gave no attention. His serological examination now was entirely negative, save that the cerebrospinal fluid contained 17 cells to the cubic millimeter. In such a case it is practically impossible to make the differential diagnosis. He does not conform to the classical disseminated sclerosis, nor, on the other hand, is there anything typical of cerebrospinal syphilis about his clinical picture, and were it not for the positive Wassermann reaction in the serum found repeatedly at different laboratories could that diagnosis be maintained.

The Brown-Séquard syndrome is not so rare a manifestation of spinal syphilis to make it of interest to report such condition. In one of the cases in this series it was rather unusual. A mechanic, aged thirty-four years, who had had a chancre when he was twenty,

had been complaining of upward of a year of a numb, heavy sensation in the right leg and a sensation as if something were running through it. He had noted latterly that he could not distinguish between hot and cold in this leg. He complained also of a jumping restless sensation in both lower extremities and of weakness of the left lower extremity. On inquiry it was found that in reality he had become paraplegic about two and a half years before and the condition for which he sought relief was in reality the sequelæ of it. The objective examination revealed anesthesia and analgesia from the fifth dorsal segment downward on the right side and of weakness of the left lower extremity accompanied by increase of the tendon-jerks on that side. His serum Wassermann was positive and the cerebrospinal fluid negative throughout. In this case the Brown-Séquard paralysis was merely a sequelæ of a meningomyelitis displaying itself in transverse lesion.

There are two cases of poliomyelitis, both adults, in our statistics. Whether these are cases of syphilitic poliomyelitis or of epidemic poliomyelitis occurring in a syphilitic individual seems to me impossible to say, but my conjecture would favor the latter view. For instance, an Italian laborer, aged thirty years, was taken ill suddenly and soon had a high fever; at the end of two days the fever was less intense and the left lower extremity was completely paralyzed. Six days later the right shoulder began to be painful and shortly afterward this extremity became paralyzed. He regained the use of the upper extremity and on examination showed comparatively slight atrophy. The lower extremity, however, showed the typical appearance of former poliomyelitis: dangle knee and ankle-joints. The tendon-jerks in this extremity naturally were not elicitable, but they also were not elicitable in the right lower extremity, which had never been affected. The pupils were irregular in contour, uneven and displayed the Argyll-Robertson phenomenon. The serum Wassermann was plus and the cerebrospinal fluid negative throughout. In the absence of a history of syphilitic infection, were it not for the positive Wassermann of the serum and the Argyll-Robertson pupils there would be no suspicion aroused that the disease was other than an example of ordinary poliomyelitis.

It is even more difficult to decide a case such as the following:

A school girl, aged thirteen and a half years, complained of headache and pain in her chest and in the back; this lasted two or three days and she returned to school. Two weeks later she complained of pain and drawing in her feet, and before the end of the day she had to be helped home from school. The next two days she lay around the house and then went to bed because she was unable to get about without help. Examination four days later revealed that she was unable to stand securely without assistance. There was generalized weakness of the legs and arms, no distinct

atrophy; the tendon-jerks were all absent; there was no tenderness of the muscles or nerves; there was no Kernig's sign and no sensory disturbance. Pupils were normal; no reaction of degeneration but distinct hypo-excitability to both currents.

Laboratory report: serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin plus, cells 4, Fehling's plus.

She recovered under salvarsan and mercury medication. The tendon-jerks of the lower extremities never became elicitable. The subject of progressive muscular atrophies dependent upon syphilitic lesion has already been presented by me before this Association, so I shall make no further reference to it.

In our series of cases there were a number of instances of facial paralysis and trigeminal neuralgia in which the blood gave a positive Wassermann reaction and the patients recovered under anti-syphilitic treatment. As has been said in another connection, it need not necessarily be that these are examples of syphilitic disease.

In many of these cases of neuralgia it was obvious from consideration of the symptoms and their response to treatment that other factors than syphilis may have had causative relationship, and particularly dental infections.

A travelling salesman, aged fifty-two years, who got infected with syphilis when nineteen and who received prolonged mercury and iodine treatment, had complained for nine months of severe pain in the left shoulder, continuous but subject to intense exacerbation when the pain radiated down the arm and up the neck. Besides he complained of numbness in the left ulnar distribution. Examination showed in addition to tenderness over the brachial plexus Argyll-Robertson pupils; roentgen-ray examination of the teeth showed three large abscesses and one extensive pus cavity in the root of a tooth that was supposed to have been extracted. The laboratory examination: serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin plus, cells plus, Fehling's plus.

Within a week after the teeth containing the abscesses were removed, and the pyorrhea overcome, the pain disappeared, though he had received but one intravenous injection of salvarsan.

In view of our ignorance of the pathogenic properties of *Spirocheta buccalis*, *Treponema macrodentium* and *Treponema microdentium mucosum*, we can only conjecture what part they played, if any, in causing these symptoms. The patient, however, completely recovered under salvarsan medication.

For a long time it was a matter of contention whether or not syphilis produced multiple neuritis. It seems to have been definitely established that it can, but that such cases are extremely uncommon is shown by these statistics. However, now and then we encounter a fairly classical example. An Italian laborer, aged forty-two years, who used alcohol very moderately, became ill a month before he came to the hospital, with vomiting, which lasted about

four days. When the vomiting ceased he began to have pains in the soles of the feet, pins-and-needles sensation in the knees, weakness of the lower extremities, giving way of the knees, and soon after of pins-and-needles sensation in the finger-tips, associated with a sensation of numbness. He soon began to find difficulty in buttoning his clothes and using a knife and fork dexterously. The affection of the lower extremities increased so that he had much difficulty in walking. Examination showed feeble gait, uncertain station, tremor of the outstretched fingers, absent knee- and ankle-jerks, atrophy of the lower extremities, more marked in the anterior tibial group of muscles, tenderness on pressure over the nerve trunks, of the extremities and symmetrical hypesthesia. The pupils were normal. Blood serum Wassermann positive, cerebrospinal fluid negative.

Again, it must be admitted that this is a case of multiple neuritis occurring in a syphilitic individual, whether or not we are justified in calling it syphilitic multiple neuritis cannot be said. In the absence of the ordinary causes of neuritis, such as alcohol and infection, it can be surmised only.

I quote an example of a case in which the diagnosis of rheumatism is made. A married man, aged thirty-four years, occupied as a packer, complained that eight weeks before he came to me he was suddenly taken with pain and swelling in the right ankle. In about two days the left shoulder and then the right wrist became involved, and a few days later the right shoulder and finally the left wrist became affected. Aside from that he had no other complaint. He denied syphilis but admitted gonorrhoea a year previously. There was no evidence of syphilitic disease, save sluggishness of the pupils to light. Laboratory examination: serum Wassermann plus, cerebrospinal fluid plus, globulin weakly plus, cells 253, Fehling's plus.

Whether this is a case of rheumatism occurring in a syphilitic individual or whether it is a syphilitic rheumatism every physician will have to decide for himself. It might meanwhile be said that the patient made rapid recovery under the administration of salvarsan and baking to the joints and appropriate diet.

Perhaps there is nothing more astonishing than to find on examination of the cerebrospinal fluid evidences of intense infection in an individual who has practically no symptoms. I saw in January, 1916, a mechanic, aged thirty-five years, who maintained that he was not ill. He had had a chancre when he was twenty years old and he wanted to be assured that he was in good condition. On direct questioning he admitted that he had at times indefinite queer sensations in the head as if he were going to have headache, and that occasionally he felt "slightly faint." The only objective sign was the Argyll-Robertson pupil. Serological examination:

serum Wassermann plus, cerebrospinal fluid (Wassermann) plus, globulin plus, cells 56, Fehling's plus.

His laboratory reports became negative under intensive treatment, but a year after the cessation of such treatment they were positive again.

The diagnosis of syphilis of the central nervous system is not such a cut-and-dried mechanical matter as one might infer from reading accounts of cases that have offered difficulties of interpretation. We encounter not a few cases in which, despite the most searching and repeated examination, it is impossible to say satisfactorily what the disorder really is. I have in mind particularly the case of a negress, aged thirty-eight years, who entered the hospital complaining of pain and numbness in the right upper extremity extending from the hand to the shoulder and radiating around the back and chest. This pain, which was continuous but subject to exacerbation, she had had about four months. Aside from impaired strength in the right hand there was no other complaint. Physical examination revealed pain on pressure over the right brachial plexus and hyperesthesia in the domain of the radial nerve. The serum Wassermann was negative on the first examination, but on three successive examinations and in two different laboratories it was positive. The cerebrospinal fluid showed no abnormalities save an excess of globulin. The blood showed nothing abnormal save a low hemoglobin index and the stomach contents were normal save for mild subacidity. She was put on general tonic treatment, including glandular extracts, and for a while she felt better, but two months later she was complaining of paresthesia and numbness of the feet. These symptoms increased in severity until they overshadowed the pain and paresthesia in the right upper extremity. After a few weeks' stay in the hospital she felt better, but after two months she was back again complaining of the same symptoms, and in addition a sense of constriction around the waist, of heaviness in the legs as though they were paralyzed, of distress in the rectum and of general malaise. Again her serum Wassermann was found positive. There was no objective evidence of disease. She received several doses of salvarsan and much mercurial treatment. The serum Wassermann became negative, but she admitted very little improvement. In the discharge note of September 13, 1915, it is noted that she still complained of a band-like sensation of numbness and tingling in her lower extremities and of a sensation as if she were walking on something soft, of pain in her shoulder and of general weakness. In March she was in the hospital again, complaining of severe pain in both arms, associated with a drawing, pulling sensation; of an aggravating, exhausting pain in the thighs; the legs felt like lead; station and gait were feeble and she had difficulty in climbing stairs. Examination showed uncertain station, moderately ataxic gait, defi-

nite loss of postural sense in the lower extremities, but no disturbance of superficial sensibility. The tendon-jerks and superficial reflexes were quite normal.

Examination of the blood showed no morphological alterations.

A roentgen-ray of the teeth failed to reveal abscess cavities. The urine showed nothing abnormal.

Six months later she was admitted again with the same complaint. She had now become thoroughly demoralized and her conduct was what is commonly called hysterical. The results of physical examination were now somewhat different from previous ones. There was distinct ataxia of the lower extremities, the tendon-jerks were exaggerated and an exhaustible clonus was elicitable. The Babinski phenomenon existed in the right foot, and neither the abdominal nor epigastric reflexes could be elicited. There was distinct disturbance of postural sensibility in the lower extremities and slight general tenderness of the lower extremities in both nerves and muscles. There was no disturbance of cutaneous sensibility. She cried and moaned, insisting she was suffering terribly and that nothing gave her any relief. The physician who took care of her after she left the hospital informed me that she grew rapidly worse and died suddenly two months later. She continued to have pain in both legs and lower abdomen without loss of reflexes and without apparent paralysis. Her emaciation and weakness was progressive, and she finally lost control of both rectum and bladder. She died suddenly about eighteen months after the beginning of her symptoms. Were it not for the positive Wassermann there was nothing in this case particularly to suggest syphilis of the nervous system, save that one husband had had syphilis, that she had had one miscarriage and that she was a negress. The course of the disease and its termination in sudden death suggests syphilis, but it is very difficult to conjecture what the pathological process was. Had we not been in possession of the information given by repeated examination of the blood we might be inclined to look upon the disease as a combined sclerosis of hemic origin.

The gist of this presentation is that syphilis of the nervous system may and often does cause the symptoms of practically every disease of the nervous system. The practical application of the conclusion is that no one can be sure that syphilis may not be an etiological factor until after laboratory investigation has been done. Syphilis invades the nervous system and often disorders it without producing the most constant pathognomonic sign, namely, loss of circularity of the pupils and impaired response to light and shadow. The sure way of curing syphilis of the nervous system is to prevent it.

"PUDENDAL HERNIA."

By ALEXIS V. MOSCHCOWITZ, M.D.,

ATTENDING SURGEON TO MT. SINAI HOSPITAL; PROFESSOR OF CLINICAL SURGERY,
COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

EARLY in the nineteenth century Sir Astley Cooper described for the first time a hernia to which he gave the name of "pudendal hernia." As the name implies, this hernia is located in the region of the pudendum. This name is, however, incorrect for the following reasons: (1) because the name does not sufficiently differentiate a pudendal hernia from the very common oblique inguinal herniæ of large dimensions, which also occupy the pudendum, and (2) because, contrary to our usual custom, the name is derived from the ultimate resting place of hernia and not from the point of its escape out of the abdomen. A much more preferable name would be "subpubic hernia," a name first proposed by von Winckel and one which describes the salient point of the hernia, namely, that it escapes behind or underneath the pubic bone even in the absence of any other descriptive qualifications. In spite of the great rarity of this hernia the name appears to be universally adopted, and it is hardly worth while to make very strenuous efforts to change it.

A number of years ago there was referred to me a patient with a pudendal hernia who had undergone the usual vicissitudes attending the treatment of such herniæ. I have refrained from publishing the case before because I wished to report in addition to the hernia also the late result of an operation of a somewhat novel nature:

Mrs. E. L., aged forty-one years, was referred to me by Dr. S. Steiner, May 15, 1913. The history prior to 1895 is irrelevant. The patient was delivered by forceps November 18, 1895, at the termination of the first pregnancy. The indication for the use of the forceps is not quite evident to me because the pelvis and all its diameters are apparently of ample size. Shortly after delivery a mass protruded from the vagina, and coincidentally with it an incontinence of the bladder was also noted. The condition was at first looked upon as one of paralysis of the bladder and a good prognosis was given. The condition, however, did not improve, and after being seen by a number of consultants she finally came into the care of Dr. F. Lange, formerly of this city, who diagnosed for the first time a vaginal rupture of the bladder, with complete loss of the urethra and also an ununited fracture of the left pubic bone. Since that time the patient was operated on a number of times. I will mention here only those operations of a major nature:

The first major operation was undertaken December 30, 1895, and surprisingly was perhaps the one followed by the greatest amount

of success. It consisted in a closure of the defect of the bladder and the formation of a new urethra out of the left labium minus. After this operation the patient regained control of the bladder.

The second major operation was undertaken May 10, 1896. The previously mentioned vaginal protrusion, which the operator recognized as a hernia, was pushed back and the opening closed by some sort of a vaginal plastic. This operation was not in the least successful; the hernial protrusion recurred immediately, whereupon the patient was informed that before another attempt at its radical cure could be made it would be absolutely necessary to first repair the fracture of the pubis.

The third major operation was therefore undertaken in January, 1897. The patient was told that the ends of the fractured pubic bone were refreshed and sutured with silver wire. Unfortunately the wound became infected and had to be reopened. Intractable sinuses formed throughout the length of the incision until the silver sutures were removed about six months later; at the same time another unsuccessful attempt was made to cure the hernia by a vaginal operation. This may therefore be called the fourth operation.

A fifth unsuccessful attempt at a cure was undertaken in June, 1899.

Thereafter the patient abandoned all hope at a cure for nine years.

In 1908 the patient again became pregnant and was delivered prematurely by a breech presentation. After this confinement the hernia increased markedly in size; it also became evident, for the first time, that the hernia contained not only the bladder but also intestines. The patient was a total invalid; she became bed-ridden and suffered a great deal of pain and untold inconvenience from the hernial protrusion; a particularly annoying symptom was the inability to empty her bladder unless she first reduced the hernia manually.

She therefore readily consented to a sixth attempt at a cure, which was undertaken March 31, 1913, by Dr. Robert Abbe, to whom I am indebted for the following notes: This operation was the first attempt at a cure by the abdominal route. The hernia in the depth of the pelvis was exposed; its contents were found to be the bladder and about three feet of small intestines. These as well as the hernial sac were drawn back, and after putting the sac on the stretch to the utmost, the opening was repaired by a sort of cystopexy, the bladder being fixed by six sutures of Pagenstecher linen to the peritoneum and fascia of the anterior abdominal wall. For a while this seemed to fulfil the intended design; however, soon after the patient was permitted to be up and about the condition recurred.

I saw the patient for the first time May 15, 1913. My physical examination revealed the following status: A well-healed median abdominal scar. A protrusion in the left labium, about the size of an

adult fist was noted; this protrusion was dull on percussion and imparted an impression of translucency; it was reducible, but upon the slightest attempts at reduction the patient felt an uncontrollable desire to urinate. The swelling was so large that its mesial surface, having pulled the vagina down, was covered with mucous membrane. The introitus vaginae was crescentic, with the convexity toward the right. The left labium minus was absent (result of previous operations). The vestibule of the vagina was so distorted that at first I was entirely unable to find any urethra; finally, after a great deal of search, I was able to discern an orifice or, better said, the opening of a fistulous tract high up, hidden underneath the symphysis, which on probing led in a tortuous manner upward and to the left into the bladder. The entire vagina was occupied by a protrusion which came down along its left side. When the mass was reduced there was to be felt to the inner side of the descending ramus of the pubis a longitudinal hiatus, easily admitting four fingers. The internal organs were negative to palpation.

The history and the physical findings were not very encouraging for a radical cure. The patient, however, was so willing, and even insisting, that I finally acquiesced to her pleadings and consented to make another attempt in a manner not hitherto tried.

This operation was performed May 27, 1913. Median laparotomy extending from the symphysis pubis to one inch above the umbilicus. Massive adhesions were encountered at the site of the last operation. After liberating the adhesions it was seen that the hernia was of the sliding variety, involving the left half of the bladder. This was very discouraging, because at the very outset it prevented me from at least extirpating in a thorough manner the hernial sac, as I had hoped to do. The small intestines were adherent in the depth of the sac and were freed.

The hernial ring was a large, irregular oval, easily admitting the folded hand, and was bounded externally by the ascending ramus of the pubis and mesially by the soft tissues of the bladder, uterus and vagina. The problem of a cure therefore resolved itself into the question of my ability to close this opening; neither pelvic fascia nor levator ani were available. I believe both were ruthlessly torn away at the original forceps delivery. I therefore deliberately carried out an operation I had evolved in advance, namely, to dislocate the uterus and to use it as a plug for the hernial opening.

In order to enable me to do so I first extirpated the right ovary and both tubes. After incising the pelvic peritoneum anterior to the left broad ligament the uterus was dislocated into an extreme sinistroversion and fastened in its new position with a number of Pagenstecher sutures to the descending ramus of the pubis. Had the uterus been only a trifle larger or the hernial ring only a trifle smaller it would have been possible to close the hernial ring completely; as it was, the lateral portion only could be obliterated, and no

matter what I did there still remained a weak area to the right of the dislocated uterus which could not be closed. The best I could do under the circumstances was to pull up the vagina and bladder and suture these organs to the dislocated uterus. The duration of the operation was two hours. The convalescence was exceedingly stormy; the patient vomited almost continually for a number of days. Temperature and pulse, however, remained normal. Primary union resulted and the patient was discharged June 19, 1913.

I kept the patient under observation, and for some time after the operation she was quite comfortable. However, about one year after operation I found on examination that the uterus was again in its normal vertical position, no more sinistroverted, and that there was again a hernial bulging. I heard from the patient the last time, just one year ago, at which time the hernia had recurred to practically its former dimensions.

As is seen I was not any more successful in curing the patient than my predecessors. This is due to a number of causes: (1) because my case was a traumatic one and that in consequence the hernial opening was of such dimensions that it simply could not be closed up with any one of the tissues normally present and normally available for the plastic part of the operation. It is on that account that I thought of utilizing the uterus, so to say, as a plug to stop up the hernial opening. It is true I finished the operation as originally planned, but already during the operation it was seen that the uterus was not large enough to completely close up the hiatus in the pelvic floor; no matter how the sutures were applied or how strongly the uterus was sinistroverted, there always remained a small opening anteriorly, which invited a recurrence. In addition subsequent events show also the fallacy of the operation, as the uterus did not stay permanently fixed in its new position, in spite of the fact that an unabsorbable suture material was used. Within a year's time the sutures had evidently cut through, as the uterus was found to have returned to its normal position. The mediocre ultimate result was, I believe, due to the extensive pelvic denudation, and deposit of cicatricial tissue.

Pudendal hernia is one of the rarest forms of hernia. After a careful search of the literature I have been able to find only the following valid cases:

Cooper,¹ in his treatise on *hernia*, devotes a special chapter to the subject of pudendal hernia, and describes the following two cases:

CASE I (Cooper).—This case was a female, aged twenty-two years, who had a hernia, the size of a pigeon's egg, for a long time, and which she had always been able to reduce. When Cooper saw the patient he found a swelling, situated below the middle of the

¹The Anatomy and Surgical Treatment of Crural and Umbilical Hernia, etc., London, 1807.

labium, while the upper part of the labium and the inguinal ring were free from any swelling. The tumor extended upward and alongside of the vagina, nearly as far as the uterine os. The hernia gave an impulse on coughing. Cooper succeeded in reducing the hernia by taxis; in doing so the hernia disappeared upward with a gurgling noise, with relief of all the symptoms. After reduction of the contents the labium was flaccid and a finger introduced into this flaccid sac could be passed upward into a circular orifice on the inner side of the ischium, between it and the vagina. Subsequently a T-bandage was used to retain the hernia.

Epicrisis. I have copied this history practically verbatim from Cooper. In spite of the brevity of the report there is not the slightest doubt that the case is a true case of pudendal hernia. It is regrettable that the anatomy of the hernial ring is not described in more detail.

CASE II (Cooper).—This case is merely mentioned in connection with the former; the report of the same is even shorter. It also was in a female who had a tumor similar to but smaller than the preceding and situated in the right labium. It disappeared in the recumbent posture but reappeared promptly when the patient stood up. It dilated on coughing.

Even before Cooper's time I find recorded 2 cases which may have been cases of pudendal hernia. All writers upon the subject of pelvic herniæ in general quote both cases as perineal hernia; the description is not sufficient to enable me to decide the question definitely. For the sake of completeness I have deemed it best to include them in my list of cases, but have decided to at least signify my doubt in their validity with a question mark. The 2 cases are the following:

CASE III (?) (Méry²).—The hernia was found in a female five or six months pregnant; it was somewhat larger than an egg and disappeared on compression. The contents were evidently bladder.

Epicrisis. Von Winckel includes this case in his list of pudendal herniæ. He, however, doubts the correctness of his action, as he adds that the description of the case is not sufficient to differentiate it from an ordinary vaginal cystocele.

CASE IV (?) (Curad³).—The patient was a female, aged twenty-three years, who was six months pregnant. On examination a lateral perineal tumor was found which increased in size on standing or when the patient refrained from urinating for a long time. It was soft and painless. When compressed manually there arose a desire to urinate, and if pressure was continued urine was actually pressed out. After confinement the hernia disappeared, but it returned in

² Mém. de l'acad. royale des sciences pour l'annee, 1739. Original not obtainable. History is abstracted from Ribes. Dictionnaire des sciences médicales, xl, 384.

³ Mémoires de l'acad. royale de chir., 1769, ii, 25.

a subsequent pregnancy. Curade states that he has no doubt that the case was one of perineal hernia.

Epicrisis. The case was either perineal or it was vesical; it could hardly have been both. The description of the physical signs and the findings are so accurate, however, and all point so strongly toward an involvement of the bladder, that I am more inclined to disregard the word perineal used in connection with the case and to place it among the pudendal herniæ.

Chronologically the next case to be reported is that of a contemporary of Cooper, and of a surgeon who has also done much to further our knowledge of the subject of hernia. I refer to Cloquet.

CASE V (J. Cloquet⁴).—Under the title “*Sur une Hernie Vulvaire*” this author publishes the following case: The patient was a female, aged twenty-four years, who complained of a swelling in the vulva. On examination Cloquet found in the posterior part of the right labium majus a round swelling the size of a large chestnut, which stretched the overlying skin and also extended toward the inner surface of the external genitals; the swelling was slightly tender and extended upward alongside the vagina; it became much more tense on standing and coughing and gradually increased in size. The patient noticed a swelling for the first time only fourteen days previously, and she believes that it was caused by straining at her work and at stool. Cloquet was able to reduce the swelling by taxis, the reduction being accompanied by a gurgling sound. After reduction a finger could be invaginated into the labium, whereupon a rounded opening was noticed between the vagina and the ramus of the ischium. Nothing further was done, but the patient immediately felt relief of her symptoms, nor has the hernia recurred since.

CASE VI (Hartman⁵).—This operator reports that he has performed an autopsy upon the body of a female who had suffered for a long time with symptoms of a vesical calculus. At the autopsy there was found a tumor in the labium which was formed by a prolapsed portion of the bladder.

Epicrisis. It is regrettable that exact autopsy findings are lacking in this case; on that account it is very difficult to differentiate it with precision from an ordinary cystocele.

CASE VII (Hager⁶).—This surgeon, under the caption “*Vorderer Mittelfleischbruch bei einem Weibe*,” describes the following case: The patient was a female, aged twenty-eight years. During her first confinement, which was very difficult, the patient noticed in the middle of the right labium majus a swelling the size of a walnut;

⁴ *Nouveau Jour. de méd.* Redigée par M. Beclard, Chomel, etc. April, 1821, x, 427. Original not obtainable. History is abstracted after Ebner. *Deutsch. Ztschr. f. Chir.*, 1887, xxvi, 101.

⁵ *Ephemerid naturæ curiosorum.* Observatio 71. Original not obtainable. History is abstracted after Jacobson. *Gräfe und Walther's Jour. d. Chir.*, 1826, ix, 399.

⁶ *Brüche und Vorfälle*, Wien, 1834, p. 297.

it decreased in size in the recumbent posture but became larger on standing and walking; it was easily replaced but reappeared promptly. The swelling increased slowly in size during the subsequent four years and then increased suddenly and became painful and softer. Poultices were applied, whereupon the swelling opened spontaneously at two points, discharged a large quantity of blackish fluid and decreased in size. Seven months later, in the course of a second pregnancy, the swelling became more annoying, on which account the patient entered Hager's clinic. At the examination there was found a swelling the size of a pigeon's egg, which occupied the right labium majus. The labium majus had disappeared by being stretched over the tumor. The vagina was pushed over to the opposite side by the pedicle of the swelling, which passed upward between the vagina and the ascending ramus of the ischium. The swelling was very tense and elastic and both painful and tender. Hager diagnosed an anterior perineal hernia (pudental) which was inflamed and also mildly incarcerated. Under local treatment these symptoms disappeared and finally the patient was discharged just prior to full-term delivery.

CASE VIII (Koenig⁷).—Speaking of pelvic herniæ, this author says that the most frequent form are those which descend alongside the vagina, in front of the transversus perinei, and then make their appearance upon the surface in the labium majus. He saw one such case, which had the size of a man's head. Detailed description is not given.

CASE IX (VON WINCKEL^{8 9}).—In this case the patient was a female who had been confined a number of times; all deliveries were very difficult; the last time instruments (forceps) had been used. Even prior to this last confinement the patient noticed a swelling in the right labium majus. Upon the mesial surface of this swelling another smaller swelling formed, which also increased in size and made quite a projection. On examination a swelling larger than an adult fist was seen occupying the vulva, and more particularly the posterior part of the right labium majus. It was situated anteriorly and to the right of the perineal body, and was bounded externally by the tuberosity of the ischium and anteriorly by the right half of the symphysis pubis. Even on casual inspection it was seen that the swelling was made up of two different parts, namely, an outer one belonging to the labium and an inner one belonging to the introitus. On careful examination the smaller inner swelling was recognized to be the everted Bartholinian gland. In the larger portion, or hernia proper, various structures could be palpated. By manipulation and pressure along the right side of the vagina most of the hernial contents could be replaced into the pelvis; one smaller body, which was taken to be

⁷ Lehrbuch der speciellen Chirurgie, Berlin, 1877, p. 201.

⁸ Pathologie der weiblichen Sexual Organe, Leipzig, 1881, p. 282.

⁹ Samml. klin. Vortr., No. 397.

the ovary, could not be replaced. Treatment with a pessary and a truss was tried first but was absolutely unsuccessful; von Winckel therefore tried a plastic operation per vaginam, which was followed by a slight improvement, but failed at a cure.

Von Winckel reviews the published cases of pudendal hernia and reports the following additional case.

CASE X.—This patient was a female, aged fifty-one years. At the age of twenty-two years, after being in labor for three days and after many attempts at delivery with forceps, she was delivered by perforation. At the age of forty-six years she noticed accidentally a swelling in the right labium, which gave rise to very few symptoms in the beginning, but did so subsequently. The swelling was reducible, and when reduced an opening could be palpated underneath the symphysis. Von Winckel made many attempts to treat the patient with a truss, but without avail, and in consequence he decided to operate.

The operation was carried out in the following manner: Through a median laparotomy it was ascertained that the intestines were so adherent to the sac that they could not be liberated; therefore the proposed closure of the sac from within the abdomen was abandoned and a ventrofixation of the uterus substituted. For a short while the condition was improved somewhat, but as a recurrence followed very soon the patient was operated a second time. At this operation the sac was split open from below, the contents were reduced and the sac obliterated by suture. The patient was greatly improved by this operation, but not cured completely; a small hernia still remained, which grew only slightly during the next fifteen years.

Von Winckel discusses pudendal herniæ from an etiological point of view and arrives at the conclusion that they are either acquired or congenital. As a case of congenital pelvic hernia he quotes the case of Lacoste.¹⁰ The case was that of a child, aged one and a half months, that had a protrusion "through" the sacrum, opposite the second spinous process, about one and a half inches above the anus. It was the size of a walnut and became more prominent on coughing or crying. In the course of time the opening in the sacrum closed by bone and the hernia disappeared.

Epicrisis. I have deemed it preferable to exclude this case as a true case of pudendal hernia, owing to its meager description and also because I believe that both etiological and anatomically the case was more likely a meningocele upon the basis of a spina bifida.

Fortified by this case von Winckel reports as a congenital hernia the following case of a male child who at the age of seven days presented alongside the left pubis and in close proximity to the scrotum, an elevation the size of a pigeon's egg, in which intestines were palpable and which were reducible. As in many other cases of

¹⁰ Froyep's Noticen, 1823, iv, 223.

puddental hernia this case also suffers from the fact that it is insufficiently described; at best it may be said that the case is not fully proved, and for that reason it might be better to exclude it. As it is the case would be the only case of a pudental hernia in a male, the only one that occurred in a child, and the only one that occurred spontaneously.

A study of these 11 existing cases enables us to make the following deductions:

1. *Sex.* I have been unable to find a single authentic case of a pudental hernia in the male. It must be said, however, that I do not accept as proved the case reported by von Winckel, which occurred in a male infant seven days old.

2. *Age.* The youngest patient recorded was aged twenty-two years (Cooper's Case I); the oldest patient recorded was aged fifty-one years (von Winckel's Case II), but this patient had had a hernia for a number of years before consulting a physician regarding her ailment.

3. *Side Affected.* In 5 cases the hernia was upon the right side; in 2 cases the hernia was upon the left side, while in 4 cases the side affected is not stated.

4. *Etiology.* Primarily, I presume all those factors which bear upon the etiology of every hernia must be considered to be effective also in pudental hernia. In addition, however, pregnancy and parturition are evidently of considerable importance in the etiology of this particular hernia. We find, for instance, that in a goodly proportion of the cases it is distinctly stated that the hernia either began during labor, or was noted very soon thereafter. In a few of the latter it is particularly emphasized that the labor was very difficult and often also instrumental, so that the presumption is very strong that the act of parturition and the trauma coincident to it had something to do with originating the hernia.

5. *Surgical Anatomy.* A pudental hernia makes its escape from the pelvis through an irregular triangular space, which, roughly speaking, is bounded laterally by the descending ramus of the pubis, and perhaps slightly also by the ascending ramus of the ischium, mesially by the vagina, and posteriorly by the transversus perinei. The latter muscle is a very important landmark, because it serves to differentiate a pudental hernia from a perineal hernia. The space is marked off by three small muscles, namely, externally the ischiocavernosus, internally the constrictor cunei and posteriorly the transversus perinei. Even in a perfectly normal individual this space is a weak part of the pelvic diaphragm.

The internal approach to this space is also somewhat triangular and is bounded mesially by the uterus and bladder, externally by the round ligament, while the base is formed by the linea terminalis of the pelvis. This is approximately the surgical anatomy of a spontaneous pudental hernia. We have seen, however, that a number of the

reported cases of pudendal hernia were traumatic in nature, the trauma being the act of parturition. What the exact nature of the trauma is it is rather difficult to determine in view of the absence of exact dissections. Judging merely from the nature of the resulting hernia the surgical anatomy can be only guessed at and appears to be a transversely running tear through the levator ani and its two fascial layers, just posterior to the symphysis pubis.

The organ which lies in closest proximity to and practically upon the surface before described is, in the first place, the bladder; it is on this account that we find in pudendal hernia so frequently symptoms referable to the bladder. The portion of the bladder resting immediately upon this space is covered only in part by peritoneum, so that the resulting hernia is usually of a paraperitoneal variety; the sac in consequence is hardly ever a complete one, and the greatest difficulty would be encountered were one to attempt to extirpate such a sac *in toto*. In the subsequent growth of the hernia other organs may find their way into the hernia, but it appears to me to be more than plausible that these would always rest upon the prolapsed bladder. An ovary was felt in the sac by von Winckel. I am of the opinion, however, that there is a greater likelihood of the ovary falling back into the cul-de-sac of Douglas, and that being the case it would be more likely to appear in a perineal hernia.

6. *Physical Signs.* A pudendal hernia usually makes its appearance in the posterior part of the labium majus. It is more or less globular in form and, owing to the frequency with which the bladder forms its contents, it gives one an impression of translucency. The one great characteristic of a pudendal hernia is that its superficial covering is made up of that part of the labium majus which is continuous with the mucous membrane of the vagina. The consequence is that the mesial half of the hernia is covered by mucous membrane and the outer half by integument. Even herniæ of very large size never involve the anterior portion of the labium majus; this is a very important physical sign, because it serves to differentiate this hernia at once from a large inguinal hernia, which has migrated into the labium. An inguinal hernia has a neck running up into the inguinal region and is always covered only by the cutaneous portion of the labium majus. Reduction in inguinal hernia occurs upward and outward in the direction of the external inguinal ring, while in the pudendal hernia it occurs in a direction parallel with the vagina.

On superficial examination a pudendal hernia is most likely to be confounded with a large cyst of the Bartholinian gland. The latter have an identical location, are covered by the same tegumentary structures and are also translucent; they can be readily differentiated, however, by the fact that all symptoms of a hernia otherwise are lacking.

It is hardly likely that a pudendal hernia will ever be confounded with a perineal hernia. It is true that the internal opening

of the two may be very close to each other; in fact, the two are separated from each other only by the transversus perinei. It might be said, therefore, that just when a hernia is in the formative period it would be exceedingly difficult to differentiate the two. In their subsequent growth, however, they take on an entirely different direction and appear upon the surface in widely different locations, namely, in the posterior part of the labium in the pudendal hernia and upon the buttocks in the perineal; there should therefore be no difficulty in differentiating the two herniæ at a stage of full development.

7. *Treatment.* No case of pudendal hernia is on record as having been cured. Of the 11 recorded cases only 2 have been operated, namely, Cases IX and X, both by von Winckel. The case reported by me is therefore the third case in which an attempt at a radical cure has been made by operation. Attempts by means of vaginal or labial plastics must be followed by failures, as no opportunity is given to follow up the two cardinal principles underlying the radical cure of every hernia, namely, high ligation of the sac and a closure of the internal hernial ring. I am of the opinion that in spite of the difficulties which may be encountered this can best be attained by approaching the seat of the trouble by the abdominal route. It is perfectly possible, though not yet demonstrated, that in the spontaneous pudendal herniæ there is a well-defined ring, with firm enough structures surrounding such ring, *i. e.*, the levator ani and its superior and inferior fascial layers, which could be utilized for a plastic, with a fair promise of success. In the traumatic cases, however, the outlook for a radical cure is very meager indeed, as has been proved by my case also, in spite of the novel procedure attempted.

STUDIES IN CHOLELITHIASIS.

II. THE CLINICAL RELATIONSHIPS OF THE CHOLESTERINEMIA TO THE PATHOLOGICAL PROCESS.

BY ABRAHAM O. WILENSKY, M.D.,

NEW YORK,

AND

MARCUS A. ROTHSCHILD, M.D.,

NEW YORK.

(From the Pathological Laboratory of Mount Sinai Hospital.)

THIS communication will deal with the relationship of the cholesterol content of the blood to diseased conditions of the bile passages, the vast majority of these being accompanied by stone formation.

The individual blood determinations will then be compared with anatomical conditions present, and when complicating factors are present their significance will be discussed and the proper interpretation indicated. Finally, the clinical value of these laboratory determinations in the making of any individual diagnosis will be discussed.

The patients upon whom these studies were carried out were derived from the surgical services of Doctors Lilienthal, Beer, Berg, Elsberg and Moschowitz at the Mount Sinai Hospital, New York. We are indebted to all of these gentlemen for their coöperation in this work.

As indicated above, no case has been included in this series unless an accurate anatomical diagnosis, made either at operation or autopsy, was available. Wherever more than one cholesterin determination was made before operation the figures given in the tables indicates an average. These figures are expressed in terms of milligrams of cholesterin for each 100 c.c. of blood. The methods employed in making the quantitative chemical estimations were described in the introductory paper of this series.

The first table details in a general way the essential facts in all of the cases studied without any attempt having been made to correlate the findings with the pathological conditions. In all of the following tables the symbols indicating the degree of jaundice are to be interpreted as follows:

- + = subicteric tint.
- ++++ = very deep jaundice.
- ++ and +++ = intermediary degrees of jaundice.

TABLE I.

Case.	Cholesterinemia, mg. per cent.	Temperature, F.	Jaundice.
185	0.322	99.6	++++
267	0.125	101.2	
351	0.3075	100.0	
330	0.230	98.6	
202	0.2125	98.6	+
331	0.1925	101.6	
328	0.190	98.6	
184	0.2425	98.0	=
194	0.2725	102.6	
85	0.175	98.6	+
495	0.235	98.6	
143	0.200	98.6	
270	0.155	100.0	
240	0.170	100.4	
344	0.132	98.6	
302	0.125	100.4	
207	0.250	99.8	
265	0.200	99.8	
284	0.162	98.6	
260	0.209	99.0	
294	0.205	98.6	
106	0.2725	98.6	++

Case.	Cholesterinemia, mg. per cent.	Temperature, F.	Jaundice.
222	0.176	99.4	
226	0.190	98.0	+
276	0.220	99.2	
148	0.212	99.0	
254	0.242	98.8	
166	0.190	99.0	
228	0.1475	101.6	
190	0.205	99.6	
263	0.1675	98.6	
181	0.110	102.4	
177	0.220	99.2	
94	0.150		
159	0.2975	98.6	
312	0.125	99.4	
306	0.190	100.4	
244	0.163	99.0	
433	0.1725	99.0	
132	0.260		+
1	0.238	99.8	++
384	0.2075	98.6	
199	0.161	99.2	
162	0.235	...	++
501	0.130	99.0	
250	0.235	99.8	
225	0.420	100.0	+++
272	0.162	99.0	
169	0.155	100.8	
343	0.250	99.4	++++
165	0.227	99.8	++
268	0.212	99.6	-
264	0.200	99.4	
179	0.205	99.0	
151	0.215		
127	0.237	...	+
269	0.230	102.0	+
382	0.175	99.8	
473	0.1575	99.6	
119	0.2375	99.0	+
126	0.200	98.6	+
128	0.1625	98.6	
195	0.176	100.2	
"S"	0.348	98.6	
273	0.1675	99.2	
134	0.290	98.6	
172	0.155	99.8	+
147	0.212	100.0	+
178	0.2725	103.6	++++
149	0.1328	100.4	++

In the following series of tables the cholesterol content of the blood is compared with the anatomical conditions present. These represent all of the pathological conditions one meets during the course of clinical, operating-room and autopsy experience. In practically all of the cases the macroscopic diagnosis of the conditions present have been verified and amplified by histological examination. These pathological conditions are as follows:

1. Gall-bladders which show a practically normal histological structure and contain usually a thin light colored bile or more rarely a viscid darker bile. Stones also are present varying in

number and size. The gall-bladder contents are very frequently bacteriologically sterile.

2. Gall-bladders frequently dilated and showing a normal or only a slightly abnormal histological structure and containing a single stone more or less impacted in the neck of the gall-bladder or in the cystic duct. The contained bile is very thin and watery. The bacteriological examination of the gall-bladder contents frequently gives negative results.

3. Large distended gall-bladders with walls of a normal thickness or somewhat thinned out, showing histologically more or less atrophy especially of the mucous membrane. The contained stones are numerous but lie loosely in the large amount of thin bile. Stones may also be present in the hepatic or common bile ducts and the ducts themselves may also be of larger caliber than normal. It may or may not be possible to cultivate bacteria from either the contained bile or stones, or from both.

4. Gall-bladders in which infection has taken place, containing a thin pus or more rarely a thick creamy pus with stones. The walls are thickened and edematous and the mucous membrane is very frequently gangrenous. Abscesses may be present in the wall of the gall-bladder or between it and the liver bed, or more rarely in the substance of the liver a short distance away. The stones contained may be numerous, indicating that conditions correspond to groups 1 and 2, with an added infection, or only a single stone is present, indicating that a hydrops, as described in group 2, has become secondarily infected. In all of these the cystic duct usually becomes shut off. Stones may also be present in any of the ducts.

5. Gall-bladders which have shrunken to less than their normal size and whose walls show a chronic productive inflammation, frequently with areas in which a more recent inflammatory reaction has occurred. The amount of pericholecystitis varies from a minimum to excessive degrees, in which it seriously hampers the necessary cholecystectomy. The contents of the gall-bladder may consist only of stones or bile which may or may not be purulent, or both of these; or thick emulsions of cholesterolin, containing fragmentary stones, are present, and in which numerous cholesterolin crystals can be seen under the microscope. When the cystic duct is open and a probe can be passed into the hepatic and common ducts the condition represents the end-results of groups 1, 2 and 3; when the cystic duct has been obliterated the condition is the end-result of group 4. It rarely happens that the scarring and contracture has advanced so far that only a short stump represents the gall-bladder.

6. Gall-bladders corresponding to those in groups 1 and 3, and with which there is associated a swelling of the head of the pancreas. Acute hemorrhagic pancreatitis of the fulminating type is not included in this group.

7. Empyemata of the gall-bladder without stone formation.

These are pure infections, and bacteria can always be cultivated from the gall-bladder contents.

8. Gall-bladders corresponding in structure to group 5 but without stone formation. These represent the end-results of those in group 7.

The results of the quantitative chemical determinations of the cholesterol content of the blood in these groups are detailed as follows:

TABLE II.—PATHOLOGICAL GROUP 1.

	Mg., per cent.
Case No. 263, cholesterol blood content	= 0.167
94, " "	= 0.150
312, " "	= 0.125
172, " "	= 0.155

The cases grouped in Table II show normal figures for the cholesterol content of the blood.

TABLE III.—PATHOLOGICAL GROUP 2.

	Mg., per cent.
Case No. 207, cholesterol blood content	= 0.250
250, " "	= 0.235

TABLE IV.—PATHOLOGICAL GROUP 3.

	Mg., per cent.
Case No. 331, cholesterol blood content	= 0.1925
328, " "	= 0.190
143, " "	= 0.200
260, " "	= 0.209
276, " "	= 0.220
254, " "	= 0.242
166, " "	= 0.190
268, " "	= 0.212
179, " "	= 0.205
119, " "	= 0.237 (jaundiced)
134, " "	= 0.290
147, " "	= 0.212 (jaundiced)
177, " "	= 0.220
265, " "	= 0.200
151, " "	= 0.215

The cases grouped in Tables III and IV, corresponding to the pathological groups 2 and 3, are biologically of a similar order and therefore it is to be expected that the cholesterol content of the blood would show figures of approximately the same range. The figures are all high notwithstanding the fact that only two of all the patients in the series had obstruction in the common duct and were jaundiced.

TABLE V.—PATHOLOGICAL GROUP 4.

		Mg., per cent.
Case No. 194,	cholesterin blood content	= 0.2725 (in puerperium)
240,	" "	= 0.170
302,	" "	= 0.125
284,	" "	= 0.1625
148,	" "	= 0.212
228,	" "	= 0.1475
181,	" "	= 0.110
384,	" "	= 0.207 (diabetic)
169,	" "	= 0.155
264,	" "	= 0.200 (pregnant)
127,	" "	= 0.237 (jaundiced)
382,	" "	= 0.175
128,	" "	= 0.162
195,	" "	= 0.176
178,	" "	= 0.2725 (jaundiced)
149,	" "	= 0.132

This table represents the findings in pathological group 4. The cholesterin content of the blood in these cases shows a normal or subnormal range unless some complicating factor is present. The individual explanations for the hypercholesterinemia cases are as follows:

Case No. 194, patient in puerperal period.

No. 264, patient pregnant.

No. 127 and 178 had obstruction in the common duct.

No. 384, patient was a diabetic.

No. 148, we have no explanation for this last figure. Possibly some complicating factor had been overlooked or omitted from the clinical records.

TABLE VI.—PATHOLOGICAL GROUP 5.

		Mg., per cent.
Case No. 185,	cholesterin blood content	= 0.322 (jaundiced)
267,	" "	= 0.125
85,	" "	= 0.175
495,	" "	= 0.235
294,	" "	= 0.205
222,	" "	= 0.176
226,	" "	= 0.190
190,	" "	= 0.205 (pregnant)
159,	" "	= 0.297
306,	" "	= 0.190 (jaundiced)
199,	" "	= 0.161
162,	" "	= 0.235 (jaundiced)
501,	" "	= 0.130
272,	" "	= 0.162
165,	" "	= 0.227 (jaundiced)
269,	" "	= 0.230 (jaundiced)
344,	" "	= 0.132
270,	" "	= 0.155
433,	" "	= 0.1725

Table VI gives the findings for the cases in group 5. The figures vary. A few are normal but most are high. Some of the high figures are so because of complicating factors. These are as follows:

Cases Nos. 162, 165, 185, and 269 are high because of obstruction in the common duct.

No. 306 is high because of common duct obstruction plus a nephritis.

No. 190 was pregnant at the time of observation.

TABLE VII.—PATHOLOGICAL GROUP 6.

	Mg., per cent.
Case No. 202, cholesterin blood content	= 0.212
132, " "	= 0.200
225, " "	= 0.420

The figures in Table VII are uniformly high.

TABLE VIII.—PATHOLOGICAL GROUP 7.

	Mg., per cent.
Case No. 106, cholesterin blood content	= 0.272 (jaundiced)
343, " "	= 0.250 (jaundiced)
473, " "	= 0.157

TABLE IX.—PATHOLOGICAL GROUP 8.

	Mg., per cent.
Case No. 184, cholesterin blood content	= 0.2425 (jaundiced)
126, " "	= 0.200 (jaundiced)

In Tables VIII and IX are the figures for the cases in groups 7 and 8. They are usually normal unless some complicating factor is present. All of the high figures given are due to a coexisting common duct obstruction due to inflammatory swelling.

DISCUSSION. Diseased conditions of the bile passages are very liable to become associated with or initiated by disturbances in the normal physiological processes of the cholesterin metabolism, and in accordance with the pathological activities are readily divided into two classes:

1. Those without gall-stone formation.
2. Those will gall-stone formation.

The diseased condition of the bile passages may have been initiated by a bacterial infection. It may remain a purely infective process or it may cause changes in the excreted bile, with subsequent stone formation; or, as pointed out in the first paper, there may be a primary disturbance in the cholesterin metabolism leading to a precipitation of stones and finding its inception most frequently during the physiological period of pregnancy. A quiescent period may then follow, and frequently this continues, with or without symptoms, for the remainder of that particular individual's life. Recrudescences may, however, occur, perhaps frequently repeated at irregular intervals, due either to repetitions of the physiological disturbances or to renewed or complicating infection, or to both,

and occurring either independently at different times or simultaneously at the same time. In these metabolic disturbances the bile passages undergo changes either mechanically, owing to the presence of stones which act as foreign bodies or as a response to the added bacterial infection, or to the combination of these two acting together or alternately at different times.

At any given moment the state of the blood's content of cholesterol is influenced on both sides of the normal range by associated conditions of the body which may have nothing in common with the physiological processes of the cholesterol metabolism and the interpretation of any blood determination must take into account these complicating factors. These are as follows:

1. The cholesterol content of the blood is lowered:

(a) By a diet which is poor in lipoids.

(b) By the occurrence of high temperatures.

2. The cholesterol content of the blood is increased.

(a) By a diet excessively rich in lipoids.

(b) By the presence of other diseased conditions especially atherosclerosis, diabetes and nephritis.

(c) During pregnancy. The hypercholesterinemia of pregnancy usually lasts for a variable period after evacuation of the uterus.

(d) By the presence of obstruction in the common bile duct. If the obstruction, however, is not absolute, as indicated by the degree of the accompanying jaundice, the cholesterol content of the blood may not be increased. This is illustrated in Table X.

TABLE X.

Case No.	cholesterin	Mg., per cent.	(jaundice)	Temperature F.
185,	"	= 0.322	++++	99.6
202,	"	= 0.2125	+	98.6
184,	"	= 0.2425	+	98.0
106,	"	= 0.2725	++	98.6
222,	"	= 0.176	+	99.4
244,	"	= 0.163	+	99.0
1,	"	= 0.238	++	99.8
162,	"	= 0.235	++	100.0
225,	"	= 0.420	+++	100.0
343,	"	= 0.256	++++	99.4
165,	"	= 0.227	++	99.8
127,	"	= 0.237	+	
269,	"	= 0.230	+	102.0
119,	"	= 0.2375	+	
126,	"	= 0.200	+	98.6
172,	"	= 0.155	+	99.8
147,	"	= 0.212	+	100.0
178,	"	= 0.272	++++	103.6
149,	"	= 0.132	++	100.4

In the classifications given in the first half of this paper the individual tables seem to show a uniformity in the cholesterol contents of the blood for each group of cases, when all of the complicating factors detailed above are properly taken into account. The only

apparent discrepancies would be found in the cases grouped in Table VI (pathological group 5). The explanation of these apparent discrepancies lies in the natural history of these disturbances.

During our studies it has become increasingly evident that the subdivisions into groups attempted above is artificial and that these groups form a continuous progression. This has already been hinted at in describing these groups. The biological sequence of events may be one of three:

1. The pure infections illustrated best in groups 7 and 8 (Tables VIII and IX). The element of the cholesterol metabolism does not enter unless there is a complicating obstruction in the common bile duct. Only in that contingency does the cholesterol content of the blood range high. The complicating obstruction is due to swelling in the duct or to inflammatory swelling or adhesions about the duct. The affection begins as an empyema of the gall-bladder, and when repeated recrudescences of infection are permitted it terminates in the contracted and shrunken gall-bladder of group 8 (Table IX).

2. The cases that have their origin in disturbances in the cholesterol metabolism. Most often these disturbances in function are initiated by the physiological changes which accompany pregnancy. The hypercholesterinemia of pregnancy may reach such a degree that the accompanying supersaturation of blood and bile is rectified to the normal by a precipitation of stones in some portion of the bile passages, almost always the gall-bladder. This immediately furnishes the explanation for the patients with normal gall-bladders containing stones, the cholesterol contents of whose bloods are normal. At some time previous to the observation there had occurred a hypercholesterinemia which had been restored to the normal by a precipitation of stones. No further hypercholesterinemic crisis having occurred, these patients have had symptoms due to the mechanical effects of the stones acting as foreign bodies and have submitted themselves to operation at this stage. It is to be expected that the cholesterol content of the blood of such patients would be normal at the time of operation.

The original factor which had caused the hypercholesterinemia may continue, however, or may be repeated at intervals, so that at the time of observation the cholesterol content of the blood is relatively high. These are conditions exemplified in group 2 (Table III) and to a large extent in group 3 (Table IV).

3. Combinations of infection and disturbed cholesterol metabolism may occur either simultaneously or alternately and with different degrees of intensity. Depending on the factor which is paramount, or the stage of the process, or the presence or absence of complicating factors, which now become numerous, the cholesterol content of the blood is found to be below the normal, at the normal or much above the normal range. These cases are illustrated in groups 2, 3, 4 and 5 (Tables III, IV, V and VI).

The apparent discrepancies in the figures given in Table VI (group 5) are now explainable. This group represents the end-results of several other groups and the cholesterol content of the blood is found to vary as these do.

From the foregoing facts it must be conceded that in any given case the diagnostic value of any determination of the cholesterol content of the blood is a variable and dubious one. One can summarize those gall-bladder conditions in which the cholesterol content of the blood is normal as follows:

1. In the presence of stones in a normal gall-bladder, without common duct obstruction and with or without high temperatures.

2. In the presence of a chronically inflamed gall-bladder containing stones without common duct obstruction and with or without high temperatures.

3. In the presence of any of the above with incomplete obstruction of the common bile duct.

4. In the presence of an empyema of the gall-bladder, with or without stones, with low or high temperatures and with no obstruction in the common duct.

5. In conditions as in the preceding division (4), with partial or complete obstruction of the common duct.

The finding of a hypercholesterinemic condition, while usually pointing to some disturbance in the cholesterol metabolism and in the bile passages, is always subject to correction in the presence of any of those complicating factors, mentioned in the early part of this discussion, which, by themselves, are capable of increasing the cholesterol content of the blood. And when this correction is to be made it becomes difficult, if not impossible, to decide whether the entire excess of the cholesterol in the blood above the normal is due wholly or only in part to these complicating factors. The situation becomes all the more complex when it is known that it is possible to obtain hypercholesterinemic figures in other diseased conditions, some of which are herewith illustrated:

TABLE XI.

Case No.	Cholesterinemia, Mg., per cent.	Diagnosis.	Temperature, F.
224	0.190	Neurosis	98.6
243	0.265	Diabetes	98.0
369	0.200	Tuberculosis	100.2
317	0.2625	Carcinoma of liver	102.0
534	0.220	Colloid goiter	99.0
215	0.200	Nephritis	98.6
214	0.190	Nephritis	98.6
283	0.205	Phlebitis of leg	
"S"	0.325	Carcinoma of stomach	98.6
"R"	0.200	Sepsis	100.4
"TR"	0.250	Gastric ulcer	
"SW"	0.220	Chronic appendicitis	

The occurrence of a hypercholesterinemia can be used as a diagnostic factor in only one circumstance. When a distinction must be made between the jaundice due to cirrhosis of the liver and the jaundice due to common duct obstruction the finding of a hypercholesterinemic condition indicates that obstruction is present. Cirrhotic conditions uniformly give low figures for the cholesterol content of the blood.

Such a state of affairs goes to show that with gall-bladder conditions the proper interpretation of any cholesterol determination is only possible after a knowledge is obtained of the actual anatomical conditions. Only then is one enabled to reason backward and deduce the natural history of the actual pathological disturbance which underlies the entire disease. Such knowledge will then furnish scientifically correct and adequate data upon which a rational method of treatment may be based.

WAR MEDICINE

CONTRIBUTORS

- LIEUTENANT-COLONEL SIMON FLEXNER, M.C., U. S. A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U. S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- DR. RICHARD M. PEARCE, National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, U. S. N. A.
- MAJOR R. M. YERKES, Sanitary Corps, U. S. A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. McMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- DR. E. E. SOUTHARD, Director of Psychopathic Department, Boston State Hospital.
- COLONEL WARFIELD T. LONGCOPE, U. S. N. A. (Prof. Practice of Medicine, Columbia University).
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- COLONEL FREDERICK F. RUSSELL, M.C., U. S. A.
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- MAJOR A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- CAPTAIN O. H. PERRY PEPPER, M.C., U. S. A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Professor of Pediatrics, University of California).
- MAJOR FRED H. ALBEE, M.C., Director of Military Reconstruction Hospital No. 3, U. S. A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.C., U. S. A.
- MAJOR JOHN A. HARTWELL, Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- CAPTAIN RALPH PEMBERTON, M.C., U. S. A.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

THE WORK OF THE BUREAU OF TUBERCULOSIS IN FRANCE— AMERICAN RED CROSS.

By WILLIAM CHARLES WHITE,
CHIEF OF BUREAU.

WHEN the name of tuberculosis is called, those that gather for conference represent many curious stages of modern life. The large percentage of those interested are those who have come in contact with it in some intimate way or those who make their living by it, with, finally, but a small group of those interested in it as a purely scientific medical problem against which they try their brains year after year with but a minimum of success. But today it has for the first time in the history of the world come forward as one of the important problems of the wastage of man power, and so has been dignified by a new situation in its relation to the

armies of both sides. America was awakened to it by the public press which published story after story of the decimation of the French forces by this disease, and though little was said about it, save in the more technical journals, we know today that the armies of the other countries were suffering in much the same way. The French Government itself was aroused to take active steps for the provision of its soldiers with tuberculosis, and America at the same time began to raise money to help in what was reported to be such an appalling situation.

In France the Service de Sante of the Army, under Monsieur Justin Godart, Sous-Secretaire d'État, established by the end of the third year of war numerous hospitals for soldiers with tuberculosis called "Hôpitaux Sanitaires." They were largely composed of the sanatoria which, through private sources, had been providing for the civil population before the war and of former convents and schools which were utilized and turned into housing places for the consumptives. Already fifteen years before the war there had been formed by the Department of the Interior a permanent committee charged with the problem of controlling tuberculosis. In 1915, however, when the question became more acute, a new powerful central committee was formed, with the chief object of collecting and distributing funds gathered for the care of discharged soldiers with tuberculosis and further of coördinating the work of the departmental committee which had been given the direct work of dealing with these soldiers after their release from the army and Department of Interior hospitals. In addition to this the Department of the Interior in October, 1915, received permission of the government to establish a credit of 2,000,000 francs, which was raised to 5,000,000 francs in 1917. This money it used in the opening of thirty Stations Sanitaires to receive the soldiers on discharge from the Hôpitaux Sanitaires of the army and in assisting the departmental committees in the home care of these cases after their discharge from the Stations Sanitaires.

In addition to this there existed a private organization in Paris known as the "Tuberculeux de la Guerre," with Mrs. Edward Tuck as its president, Mrs. Edith Wharton as its vice-president and Mr. Blair Fairchild as its secretary, which undertook to provide a number of sanatoria for the same group of soldiers reformed on account of tuberculosis. A large part of the money for this work was raised in America, especially in Boston, through the efforts of Miss Sally Fairchild, and in New York, through Mr. Walter Maynard.

During the time that these organizations were performing their tasks the Rockefeller Foundation sent Dr. Herman Biggs to France to make a study of the situation and to report on the advisability of this Foundation undertaking an antituberculosis campaign under its supervision. As a result of Dr. Biggs's report, a com-

mission was formed, with Dr. Farrand as its director, Dr. James Alexander Miller and Dr. Selskar M. Gunn, as associate directors, who were commissioned to come to France and undertake, in coöperation with the French, a campaign against tuberculosis. Shortly before the consummation of this commission, America had entered the war and the American Red Cross announced its drive for \$100,000,000 for assistance in connection with the war in France. One of the chief appeals which it made to the people of America was for assistance in the field of tuberculosis and in preparation of its plans in carrying out this work. Mr. Homer Folks was asked to take charge of its crusade against tuberculosis, and was later made an assistant director of the Rockefeller Commission. Upon his arrival in France, in the early days of July, Major Murphy, commissioner for the American Red Cross for Western Europe, invited Mr. Folks to take charge of the whole of the work of the Department of Civil Affairs. Mr. Folks accepted this position and appointed Dr. William Charles White, who had come to France in June to take charge of the work of the Tuberculeux de la Guerre, to the position of the Chief of the Bureau of Tuberculosis. Dr. White was also made an associate director of the Rockefeller Commission. In this way all the American effort in the tuberculosis campaign in France was carefully correlated and started on its mission.

The first task was a division of labor between the Red Cross and the Rockefeller Foundation, so that their efforts would contemplate a uniformity of results. The Rockefeller Commission undertook a study of the conditions existing, the provision of dispensary service, an educational campaign and the selection of two units—one an arrondissement of Paris and another a department of France—in which it would provide a model organization to be used as an object lesson in American methods.

The Red Cross Bureau of Tuberculosis undertook the more immediate fields of the work, such as the provision of hospitals, improvements of conditions in temporary hospitals, assistance to French organizations dealing with tuberculosis and a careful study of the whole tuberculosis situation in France, which might be used in conjunction with the Foundation's work for a permanent program and lasting evidence of the work of America.

This article will deal mainly with the work of the Bureau of Tuberculosis. To present it clearly I have divided the subject into the following divisions:

1. Provision of new beds in existing French institutions.
2. Improvement of conditions in existing French institutions.
3. Provision of new hospitals for the civil population, conducted entirely by the Red Cross.
4. Coöperation with the Rockefeller Commission.
5. The establishment of a hospital admission bureau.

6. Provision of hospital for American soldiers.
7. Provision for Serbs.
8. Its permanent work of departmental reconstruction with its preliminary survey and subsidy as the basis of its future lasting effort in France.

Provision of New Beds in Existing French Institutions. Bligny Sanatorium. One of the suggestions of Dr. Biggs's report was the completion of the sanatorium at Bligny near Paris. This sanatorium at the beginning of the war already had provided by its excellent modern buildings for about 200 patients and had under more or less complete construction provision for about 350 more patients. In 1914, however, all building work in France was dropped, and where busy workmen had been employed, idleness and disuse became apparent. Grass grew about and covered the materials for construction; the iron and forges rusted and the parts of the building which should have been covered, being exposed to wind and weather, suffered from slow disintegration. Those buildings in use were later taken over by the Service de Sante of the army for the use of soldiers with tuberculosis, under Dr. Guinard, who was the medical director of the institution, and its use for the civil population was discontinued. It was in this condition that we found it in September, 1917, and following Dr. Biggs's suggestion, it was considered wise to undertake completion of those parts of the institution which were most nearly ready for occupancy. After a conference with the Service de Sante and the board of management of Bligny, visits to the institution with the architect, Mr. Vaudoyer, and our own construction department under Mr. William Emerson, it was found that an appropriation of 406,000 francs would complete the building and provide for 250 more tuberculous soldiers. Much of the material required for this completion was available under the former contracts, either on the ground or in the workshops of the contractors. This provided for the closing of the windows of the building, the completion of the tiling, the central heating plant, the equipment of the kitchen, the dining room and the terraces. The arrangements were finally consummated and work started toward the end of September, with the hope that by January patients would be admitted to the institution. This, however, did not reckon with the difficulties of construction work in France today, and it was not until March that these beds were ready for use. It was, however, perhaps as well, because in March the great new German offensive began and Bligny Sanatorium was able to take 150 soldiers—wounded and tuberculous—from a hospital evacuated because of the drive against Montdidier.

Hôpital St. Joseph. Shortly after the work was started at Bligny, Dr. A. H. Garvin, assistant chief of the Bureau of Tuberculosis, and Dr. Wyatt, in charge of the dispensary work of the

nineteenth arrondissement under the Rockefeller Foundation, found in the fourteenth arrondissement of Paris a very keen interest in the tuberculosis problem on the part of the board of management of the Hôpital St. Joseph. This institution, which is one of the largest and best hospitals in Paris, had purchased an old convent with its adjoining garden and had plans under way for reconstructing the building and utilizing it for tuberculosis hospitalization, with wards for men and women, a dispensary service, a recreation hall and day camp in adjoining buildings. The dispensary was to be conducted in conjunction with home visiting work. The war stopped all of its plans.

After consultation with the board of management it was found that if the Red Cross would contribute 285,000 francs, Hôpital St. Joseph would be able to add 208,000 francs for the completion of the building and thereby secure 250 more available beds for the civil population in and around Paris. The details of this arrangement were finally consummated.

As a result, however, of this gift a great step forward has been made in the partitioning of Paris for intensive dispensary work, for it has been possible to secure the hearty coöperation of the administration of Hôpital St. Joseph in an attempt so to divide the city that the tuberculosis work will be uniform and the different institutions dealing with the problem not overlap in their activities.

Improvement of Conditions in Existing French Institutions. In the first few months of our work in France it became apparent that the tuberculous portion of the population fell into six more or less well-defined groups, for the care of some of which new organizations had been started. These six groups are as follows:

1. Soldiers who were still under the jurisdiction of the Service de Sante of the army and cared for in the hôpitaux sanitaires. On October 31, 1917, there were 8879 of these for which the Service de Sante had provided 6521 beds in 37 hospitals. This group was composed of those who might still be of service to the army upon improvement in health.

2. Discharged soldiers of the second class whose connection with the army was completely severed and who were known as "Reformés No. 2." From August 2, 1914, to October 31, 1917, there were 80,551 soldiers discharged from the army on account of tuberculosis, and the Department of the Interior undertook to provide for their care by means of stations sanitaires and comites departementaux. The former by 3000 beds accepted patients for three months from the hôpitaux sanitaires; the latter provided individual assistance after their discharge.

3. The third group was composed of the rapatriés. These rapatriés were that portion of the population which had been engulfed by the German advance into France and Belgium, and being no longer of any economic service to Germany—the diseased

of all kinds, the old, the children, the maimed and disabled—were sent back into France. Among them were a large number of tuberculous. For the care of this group practically no provision had been made in the summer of 1916.

4. The fourth group was composed of refugees who fled before the German advance. These became naturally quickly merged in the civil population, but were taken by various organizations as separate groups, to which were given additional food, clothing, furniture and medical care. Among them also were numbers of tuberculous, and they were packed in the various cities and towns in the worst sort of sanitary conditions in any available buildings which could be made rapidly ready for their reception. No provision was made for the care of this moiety of the population.

5. The fifth group was the whole civil population of France. Practically all the institutions that had been available for them before the war were now utilized by the Service de Sante of the army, and there was nothing available for the women, children and old men suffering from tuberculosis.

6. The sixth group was composed of the refugees from other nations, chiefly Serbians and Belgians. For these France did her utmost with a generosity characteristic of her attitude, but naturally with her other burdens all she could do was inadequate.

A careful survey of the field indicated that the direction in which the Red Cross assistance could best be given was to those with whom France was having the greatest difficulty. These groups were the completely discharged soldiers, many of whom had now no longer any families, having been drafted from the devastated regions, the rapatriés, the refugees, the civil population and the foreign refugees.

With the main objective of leaving the assistance in the hands of the French who had already been organized for these various purposes, the Bureau of Tuberculosis undertook to assist the existing French organizations and hospitals for the care of the above groups. The first opportunity was presented after seeing the conditions in seven sets of barracks which had been provided by the assistance publique in connection with the large hospitals and almshouses in Paris. These barracks were temporary structures of wood and had been provided for completely discharged soldiers—Reformés No. 2—but the conditions in them were such that from lack of food and insufficient equipment the patients would not remain long. There were available in this way 1052 beds, of which only 174 were occupied. It was felt after examining them that with diet kitchens, recreations rooms, additional clothing and materials to brighten their aspect, such as bed covers and flowers, that these beds might be filled up and a division of the Bureau under Mademoiselle Noufflard, a Frenchwoman who had already won the Croix de Guerre for her services at the Front, was created for this purpose. The success of the work of Mademoiselle Noufflard and

her assistants has been remarkable. Not only has she increased the number of tuberculous patients in the barracks from 174 to 657, thus providing for the segregation of this many more consumptives, but she has been able to exert a marked influence for good on the whole policy of the assistance publique in its relation to the tuberculosis problem. New construction in the shape of cure halls, dining rooms and recreation rooms were provided by the Red Cross and at St. Antoine by Mrs. H. B. Duryea, of New York. Additional nurses were also provided at the expense of the American Red Cross.

Institutions for Tuberculosis in the Rest of France. Immediately following this division of the work for Paris a new division for institutions dealing with tuberculosis outside of Paris was created with a triple object in view:

1. To assure the French people that the American Red Cross had the desire to help in the situation.

2. To help the patients already in hospitals suffering from tuberculosis.

3. To gather an inventory of the equipment already possessed by France for the war against tuberculosis.

This new division was begun under the supervision of Dr. Garvin, the assistant chief of the bureau, and four visitors were started on a tour, department by department, over the whole of France. These visitors found that tuberculous patients were housed in the following types of institutions:

1. Hôpitaux sanitaires.

2. Stations sanitaires.

3. Hôpitaux mixtes (which formerly were civil hospitals, but now take military and civil cases).

4. Hôpitaux complémentaires (annexes to military hospitals).

5. Sanatoria.

6. Hospitals for bone and gland tuberculosis.

These provided 11,000 beds for tuberculosis of all kinds for a population of 39,500,000 people, with a total death-rate from tuberculosis in 1913 of 84,443. Many of these institutions required additional bedding, additional food and additional equipment, which the American Red Cross undertook to furnish at a cost of approximately 100,000 francs a month. It utilized, however, this assistance as a means of gaining an accurate knowledge upon which to base its future constructive work. Each visitor was given a questionnaire, carefully prepared by Dr. Baxter, assistant chief, and Miss Laws, secretary of the bureau, to be filled in under the following headings:

1. General information.

2. Admission requirements.

3. Administration and employees.

4. Physical condition of buildings and grounds.

5. Structural needs.
6. Improvements in general service for present needs.
7. Desirability of institution as a factor in departmental needs.
8. Miscellaneous local tuberculosis institutions and associations.
9. Municipal information in general.
10. Summary and recommendation.

These general headings were divided under numerous sub-headings, as for instance, under Physical Condition of Buildings and Grounds, were considered wards, sanitation, ventilation, heating, disinfection, toilets, general surroundings, etc.

As each of these reports came back to the office it was carefully analyzed and utilized as a basis for the future proposals which will be considered under the heading of "Departmental Organization" later in this article. Through this division of the work, assistance was given in five months to approximately 12,000 tuberculous patients.

A second field of work in connection with the French institution, of which there have been a number of examples, is exemplified by the assistance given to the Hôpital d'Ormesson. This was the first hospital in France for the care of tuberculous children. On April 15, 1916, it opened one of its buildings for 160 tuberculous soldiers by an arrangement with the Service de Sante for three francs per day per patient. It soon found its deficit amounted to about 10,000 francs a month, and it was unable to continue, and so notified the Service de Sante. After visitation to the hospital and seeing the excellent work that was done, an agreement was reached between the hospital board and the Service de Sante that the American Red Cross would make up the deficit and so continue the use of the 160 beds which would otherwise have been unavailable.

The Bureau of Tuberculosis was also able to help Mademoiselle Chaptal, one of the pioneers in tuberculosis work in France, to procure through her organization, by a gift equal to the amount contributed by it, a hospital of 40 beds for tuberculous women of the civil population. This type of work continues from time to time and is considered an excellent method of securing permanent provision of beds under stable organizations.

Provision of New Hospitals for the Civil Population. It soon became apparent that the most urgent need in France was the provision of institutions for the tuberculous members of the three groups of population—civil, rapatriated and refugee mentioned above. For these France had been able to do very little during this time of emergency. The Bureau of Tuberculosis, therefore, undertook to assist in this field.

It chose as its field of operation the two largest centers of population, Paris and Lyons. It received the offer from the Department of the Seine of certain properties known as Hachette and Malabry,

which this department had purchased before the war for the construction of cheap houses for working people, by a plan known as the "Garden City Plant." This work, under the direction of Henri Sellier, whose conception it was, was arrested by the beginning of the war. Mr. Sellier, however, was interested in the whole tuberculosis problem and offered the properties, free of rent, to the Bureau of Tuberculosis, to be utilized for the housing of consumptives of the refugee and repatriated portions of the population. Mr. Sellier had formerly offered the property to Mr. Brissac, Sous-Secretaire of the Department of the Interior, and to Dr. Leon Bernard, of the Comité National d'Assistance aux Anciens Militaires Tuberculeux, but owing to lack of funds it could not be used by them. After a conference with all parties concerned it was finally turned over to the Bureau of Tuberculosis of the American Red Cross, and under the direction of Dr. James L. Gamble the work of rehabilitation of the building was commenced, utilizing for the labor a group of American and English Friends.

The two properties given by the Department of the Seine for this work comprised in all about 150 acres of ground, with three large houses and a number of outbuildings. The Bureau of Tuberculosis was able to secure in the immediate neighborhood also two other large houses, rent free, for the purpose of enlarging the number of patients whom they could accommodate. Work of reparation was started on the main building toward the middle of November, and on Christmas Day following the first three refugees with tuberculosis was admitted. This number increased week by week until at the present time there are about 150 women and children refugees in the institution. The future plans for this whole property, to which the name of Edward L. Trudeau has been given as a fitting name, both to honor the greatest American physician in the tuberculosis world and to bring about a feeling of unity between the two countries based upon Dr. Trudeau's French origin, contemplate the following different groupings of people: A sanatorium for women, a detention house for entering children, a hospital for tuberculous children, a preventorium for children of tuberculous parents and a colony for families with a tuberculous member from which the sick one cannot be separated. With the completion of the project, approximately 2000 persons in which tuberculosis is a common factor will be cared for. The work is being carried out in coöperation with the Department of the Interior of the French Government, the dispensary service is of the Rockefeller Foundation and our own Hospital Admission Bureau. The economic value of gathering these various functions of the bureau in the same immediate region near Paris, its source of supply of patients, is an important one, solving many of the difficulties of transportation and central administration which are serious even in peace times but much magnified under the present war conditions.

The colony plan, or "school for housing," as it has been called, merits perhaps a paragraph of explanation. It is a new implement in the field of tuberculosis stimulated by an emergency and following somewhat the lines of the Home Hospital Plan of New York City, but in a much more economic way. Miss Helen Knight Smith, formerly of the Home Hospital Service, and Mr. John Kincaid are at the present time developing this plan. The necessity for it arises from the homeless population which comes from behind the German lines. Many of these have tuberculous members which they refuse to give up, having already lost other members through segregation by the Germans. If these were allowed to go with their tuberculous member into the housing conditions provided for repatries it would mean, naturally, many chances of infection of other portions of the population. They all, moreover, have a keen desire to return to the regions from which they have been evacuated as soon as the war is ended. They are thus a displaced and transient population. The plan of the home colony contemplates taking them during the transient period in small houses specially constructed for the care of an individual tuberculous member. Each house is composed of three rooms—two sleeping rooms and a living room—with a small porch for the consumptive member. Each family will perform its own household duties, the children will be occupied in open-air schools, those members able to work will be given vocational training, based upon the vocations most likely to enable them to earn their living when they return to their homes, such as gardening, carpentry, tailoring and shoemaking, all families will be under careful intensive instruction in hygienic living, the expenditure of the family budget, cleanliness and citizenship. Amusements will also be provided through voluntary work by those who are interested in this field. The details of this plan need not be further elaborated here, but if it be successful for the necessity which compels it, it will undoubtedly be feasible for many of our large city problems for tuberculous families at home, both from its economic aspect and from its educational value, for without question the domiciliary care of the consumptive now looms as one of the most important factors in our war against tuberculosis.

Asile Ste. Eugenie. A simpler project is under way in the next largest center of population—Lyons. Here by coöperation with the Hospice Board which controls a number of the hospitals of the city of Lyons the Bureau of Tuberculosis received, rent free, a large hospital building and five barracks for the housing of rapatries and refugees—women and children—suffering from tuberculosis. This hospital, under the charge of Lieutenant Bellis, U. S. M. R. C., was opened in November, 1916, with provision for 210 patients. A good deal of reconstruction, painting and cleaning had to be undertaken, but this was accomplished with great rapidity through the combined efforts of the Hospice Board and the Red Cross.

Lyons, situated as it is on the direct line from Evian through which the rapatriés enter France, forms a sort of clearing house for the tuberculous portion of this group. The Asile Ste. Eugénie works in conjunction with the French Bureau for the Care of Rapatriés and with the committee of Lyons which has their distribution in charge. The food and its preparation, the laundry and the equipment are all provided by the Hospice Board, the Red Cross paying a *per capita* rate per day per patient of between three and six francs based upon the cost to the Hospice Board itself. The Red Cross receives from the French Government 2.75 francs to 3.25 francs for the care of each case which it cares for, thus reducing its actual expense of operation. The Red Cross in addition provides the medical care and most of the nursing. It is planned at the present time to increase the work at Lyons to assist that portion of the civil population which is not at the present time permitted to enter the Asile Ste. Eugénie.

Coöperation with the Rockefeller Commission. As mentioned above the plans of the Rockefeller Foundation were formulated on the basis of a long-distance view of the best permanent general organization for the war against tuberculosis in France. At the beginning of its work it was necessary for it to take a very careful survey of the whole situation, and it was consequently unprepared to do the immediate types of work found to be necessary. Wherever it was necessary, however, to give additional equipment in the nineteenth arrondissement of Paris or in its model Department of Eure-et-Loire or in its educational campaign, the Bureau of Tuberculosis accepted with interest the responsibility of providing the things desired. This assistance consisted of appropriations for dispensary construction, appropriations for educational pamphlets and assistance in the provision of hospital beds.

The Hospital Admission Bureau. With the publicity which heralded the work of the Rockefeller Foundation and the American Red Cross in the field of tuberculosis in France the requests for assistance for individual cases became a prominent factor almost from the first day of our arrival in France. This was more pronounced, inasmuch as the work of the Bureau of Tuberculosis commenced by the acceptance of an already-going concern, the *Tuberculeux de la Guerre*. It was soon apparent that some special division must be established for the handling of these cases, and in conference with Dr. Miller a division known as "The Hospital Admission Bureau" was made a part of the Bureau of Tuberculosis, since this Bureau had mainly to do with this work from the hospital side. The Hospital Admission Bureau was put in charge of Miss Shackford. Special cards were drafted by Mr. Dorlet, both for admission to the institutions and later follow-up work in the dispensaries upon the discharge of the patients from the institutions.

The Hospital Admission Bureau then undertook to get in cor-

respondence with all the hospitals dealing with tuberculosis in France which had been recorded through our Division of Hospital Relief, to arrange with them for the acceptance of cases recommended by our bureau on the payment of the *per capita* cost of the institution accepting them. This *per capita* cost ranged from 4.5 to 6.5 francs per day. The Hospital Admission Bureau from December 25, 1917, to April 18, 1918, had arranged for the placing of 759 cases of tuberculosis. It is hoped that this division of the bureau will grow into a permanent implement to be left in the hands of the French who up to our coming here had not been familiar with it, and that it will continue of great service in bringing the hospitals and dispensaries into close coöperation with each other. It has of course as one of its functions to place the proper types of cases in the institution suited for them and to see that cases are not lost track of upon their departure from the hospitals. It will also be the beginning of central registration of living tuberculous cases which has not existed prior to this time in France.

Provision of Hospital for American Soldiers. After studying carefully the question of the relation of tuberculosis to the various armies that had been fighting for the first three years of the war it was decided that the American Army, no matter how careful the exclusion of tuberculosis cases in the draft, would still have to deal with a group of cases which would develop tuberculosis from existing lesions not possible of diagnosis in the examinations given prior to conscription. It was thought that this was a field of work in which the American Red Cross could render assistance to our own army here in France. It seemed quite obvious that there would appear certain pneumonic types of tuberculosis, certain acute miliary cases, some severe hemorrhagic cases, many acute pleuritic cases with effusion, and probably a number of cases with tuberculosis in other parts of the body than the lungs. It seemed quite clear, too, that it would scarcely be fair to these individual cases if acute in type to follow the general order of the army and send them home. With this thought in mind an offer was made to the army headquarters to provide a hospital to work in conjunction with the hospitals of evacuation near the shipping ports in which the Red Cross would be given permission to take care of such cases needing hospital care prior to their return home. The medical division of the army after looking into the problem found that as early as December the need for such an institution was already apparent and the offer has been accepted. The Bureau of Tuberculosis will, with the utmost speed at its command, undertake the provision of a hospital near Bordeaux, which will then be turned over to the army for its administration in the care of these acute types of cases. As the need grows it is hoped that a similar institution may be provided for the hospital at Savenay,

where most of the tuberculous soldiers are cared for at the present time in tents.

The Problem of the Serbians in France. One of the earliest problems presented to the American Red Cross was a request for assistance for tuberculous Serbian refugees in France. No exact figures could be found upon which to base such assistance, and yet there was apparently a great need to be dealt with. After searching in every available office of the Serbian representations in France and of the French Government, there was still not enough data upon which to start work. Consequently the Bureau of Tuberculosis started a division for the study of the Serbian question under Dr. Francis Georger and later Mrs. John Knox Freeman. A visit was made to all the Serbian camps in France and arrangements made for the examination in our various dispensaries of the Serbians thought to have tuberculosis. This work took a great many months, but as a result of it a complete report of existing conditions among this group has been compiled and a recommendation made for the provision of a hospital for the care of tuberculous Serbians. The French have done their utmost to help the Serbian situation, but were unable to take care of the tuberculosis situation except by the admission of a few cases to the French military hospitals. The following statistics will sum up the situation as we found it: There were 17,285 Serbian refugees in France; of these were found 400 actually tuberculous, only 32 of which were receiving sanatorium care. It is hoped that the hospital for tuberculous Serbs will be under way before the close of April.

Departmental Reorganization. The task of orienting themselves by those who came to France in the summer of 1917 to undertake the reorganization of social conditions in a foreign country with an environment and background of a world war was a very difficult one. Their mental attitude was at first one of constant comparison with the conditions at home and possibly a desire to reproduce here the organization which had been evolved in our own country. Gradually, however, the fact that it was a wholly different problem was borne in upon them.

France had a democratic central government different in many aspects from that at home. She had never approached the tuberculosis problem by governmental control prior to the war, and the work had been done mainly by voluntary organizations. The central government had changed five times during the period of the war, which left little opportunity for a permanent policy.

France is divided into departments somewhat similar to our States, with the fundamental difference, however, that the prefects, who correspond to our governors, are appointed by the Ministry of the Interior and not elected by the people. This made local autonomy in health matters under the prefect difficult. In some

large centers of population the mayor is more powerful than the prefect of the department, and by virtue of being a senator in the central government or a former minister as well as mayor he may take precedence in authority in a way not likely to occur at home. In addition to this the war made a very strong War Department which overshadowed the Department of the Interior. The latter, however, had to accept the main burden of the tuberculosis problem. Then as at home large numbers of voluntary organizations had undertaken the task of raising money and making some provision to handle the sick in hospitals and dispensaries.

The effort to steer a judicial course in this situation became more and more a task requiring the greatest tact. The mere gift of aid to those who were suffering already from tuberculosis in their homes or assistance to existing institutions was obviously not enough. There constantly presented itself to the minds of those charged with the direction of this work the demand for some definite plan to pursue with the object of leaving in the hands of the French themselves an organization which would be stable and arranged in such a way as to bring about the best results under governmental control. It was obviously impossible to do it through a changing central government.

After studying the situation, however, for many months, it was finally decided that if the work could be begun in the departmental units and a proper organization established for each department the correlation of these at a later time would probably be a comparatively easy thing. When this conclusion was reached the rearrangement of our knowledge on this basis was begun. Carefully prepared cards on which was tabulated the general knowledge gathered from each department, division of department, city or town were printed under the following headings:

Population.

Total deaths.

Deaths from tuberculosis.

Estimated living cases.

General death-rate.

Tuberculosis death-rate per 1000 from the latest available figures.

Then in two columns was shown a theoretical equipment for the control of tuberculosis under such conditions and a recommended program upon which it would be safe for the Red Cross to carry on the work with its available funds. On the back of the card was a list of the hospitals, sanatoria, dispensaries, institutions and organizations already existing. A subtraction of this latter list from the recommended program naturally formed a lead at least as to what should be done in each region. This conception finally came to be the main field of work of the bureau.

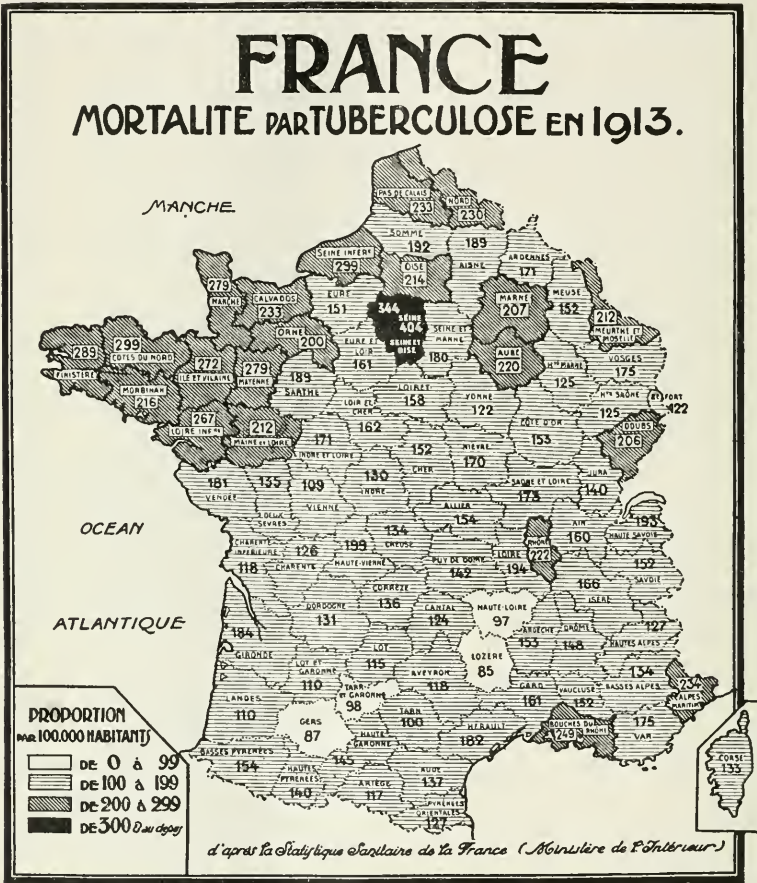
The Department of Indre-et-Loire may be taken as a typical example of the method pursued. The division of the French Red

Cross Society known as "Secours aux Blessés Militaires," with the Comte de Pourtales as the district director, appealed to the Bureau of Tuberculosis for assistance in providing a hospital for tuberculosis at Tours. There existed already, however, in that department a Comité Départemental charged with the care of the reformés, a dispensary and a day camp under other organizations. Upon the first visit of Monsieur de Pourtales he was asked if it would be possible for him to undertake the bringing together of these various organizations into one single group which would undertake, under the direction of the prefect, the handling of all tuberculosis problems in the department, and further to see what amount of money the various organizations could contribute toward a definite program. He was promised that if the organization could be consummated the American Red Cross would be willing to assist in an equal amount whatever they were able to do themselves.

With this beginning and after later conferences in Tours and Paris, the desired results were finally attained and the Red Cross agreed to give 250,000 francs toward the provision of a hospital under the following terms: That the new committee take steps to organize the existing dispensaries under its general supervision; that it plan and install other dispensaries throughout the department; that it employ salaried trained visiting nurses for the dispensaries to organize and supervise the visiting work in the various communes; that plans for providing hospital beds for advanced cases be undertaken and that the American Red Cross pledge itself to assist in this work and the other needs of the department as they arose.

In March, 1918, with the knowledge tabulated for most of the other departments in France and the success obtained in Indre-et-Loire, a new division of the Bureau of Tuberculosis was created under Mr. Frank E. Wing, who in conjunction with Dr. Alexander Bruno, of the Rockefeller Foundation, undertook the work of visiting France, department by department, with the object of proposing to them a similar plan. They began in the Departments of Loire Inferieure, Ille-et-Vilaine, Cotes-du-Nord, and Finistere. They are to visit each organization having to do with tuberculosis, such as the prefects and mayors, the comités departementaux, the three branches of the French Red Cross and all voluntary organizations dealing with tuberculosis, suggest the necessity of their coming together in a central group to accept the responsibility of all the work of the department, and as an incentive to them to do this the Bureau of Tuberculosis proposes to give them such assistance as it is able in dispensary and hospital equipment. This work will probably consume the greater part of a year or longer, but as a result it will leave a lasting impression of the American effort in France with the control of the tuberculosis problem in permanent hands in such a way that the work will continue after the necessity for the withdrawal of the American assistance.

The accompanying map prepared by Dr. Drolet will give some idea of the condition in the different departments from the stand-point of tuberculosis mortality in the year 1913, in which the last figures for such a computation were available.



It is, in general, the plan of the bureau to go first into the blackest areas, which are those in which the mortality has been highest. This work is being carried out in full coöperation with the Rockefeller Foundation, which, if the plans mature, will continue the work after the Red Cross assistance has been discontinued. The spirit in all of this work exemplifies a determination to make the assistance given to France in this epoch of her history the best expression of America's interest in the burden which she has carried so long. It is one in which all personalities have been suppressed and only an ultimate of what is best for France and her condition considered, and it is the hope of all who have been interested in it that it may meet the purpose for which the funds in America have been contributed.

The Ration and the Requirement of Food for Children.—PFAUNDLER (*München. med. Wchnschr.*, 1918, lxx, 173). In October, 1917, the civilian ration for the population of Munich contained 56.7 grams of protein, 30.5 grams of fat, 308 grams of carbohydrate and had a fuel value of 1760 calories. It was constituted as follows: Bread, 285 grams; potatoes, 500 grams; egg, 6.4 grams; meat, 35 grams; sugar, 28.6 grams; butter, 10 grams; milk, 250 c.c.; cheese, 15 grams; grits, 15 grams. The cereals contained 26 grams of the total protein, meat 7.7 grams, milk and cheese 11.7 grams, and egg 0.8 gram. This ration was not materially changed from October to January, 1918. The ration for children in the second year of life was the adult ration and $\frac{3}{4}$ liters milk, 7.1 grams sugar, 15 grams cakes, 21.4 grams grits—in all 83.4 grams of protein, 58.2 grams of fat, and 375 grams of carbohydrates, with a fuel value of 2410 calories. Pfaundler states that this is too high a value and its reduction in the following years of the child's life has had bad results and led to many complaints. Children in the third and fourth years of age received the adult ration plus 500 c.c. of milk—in all 71.7 grams of protein, 48 grams of fat, 330 grams of carbohydrates, with a fuel value of 2082 calories. Children in the fifth and sixth years received the adult ration plus 250 c.c. of milk, containing in all 64 grams of protein, 39.5 grams of fat, 319 grams of carbohydrate, and 1920 calories. After six years of age children received the normal adult ration of 1760 calories. Pfaundler gives curves of the nutritive requirements of children of various ages compiled from von Pirquet, Schlossman, Cammerer and others, showing, for example, that a child of fifteen may require 2450 (von Pirquet) or 2000 calories (Cammerer) per day, and he recasts the ration for children as follows:

Age of children.	Münich ration, October, 1917.	Pfaundler's recommendations.
1 to 3 months	943	
4 to 12 months	1133	
2d year	2410	1550
3d and 4th years	2082	1550
5th and 6th years	1920	2070
6 to 16 years	1760	2070

Pfaundler hopes that his recommendations will be followed in the interest of the rational nutrition of children. He notes that from February 4, 1918, school children of seven to fourteen years of age were given half a liter of skimmed milk in the place of a quarter of a liter of whole milk, thereby increasing the calories by 40, but reducing the quantity of butter fat. The expected improvement in the condition of the school children was not achieved by this procedure. [If it were not for this article it would appear to the abstractor incredible that the official food control of Munich, the town in which Carl von Voit had lived and taught in the fourth year of the war, should have been so ignorant as to the food requirements of children.]

G. L.

The Composition of Meat under Various Conditions of Nutrition.—DIESELHORST (*Pflüger's Arch.*, clx, 522) finds that the chemical composition of the protein structure in the muscle is independent of the

nutritive condition of the animal. The analyses are based upon the muscle substance free from fat glycogen and ash. When a dog was given rice the relation between nitrogen and carbon (N. C.) in the muscle substance was 1 to 322, and when given meat in large quantity the relation was 1 to 323. In another dog when fasting the N. C. ratio of the muscle was 3 to 188 and after partaking of a mixed diet in large quantity the ratio was found to be 1 to 3185. G. L.

Barley as a Food Material.—RUBNER (*Arch. f. Physiol.*, 1917, p. 339) says that wheat, rye and barley when milled to the same degree show little difference in absorption except that the protein in rye is a little less digestible than the protein in the other two cereals. G. L.

The Treatment of Wounds by Flavine.—PILCHER and HULL (*British Med. Jour.*, February 9, 1918) after an experience with more than 5000 cases treated by flavine, are confirmed in their good opinion of it as time passes. They have found that for ease of preparation and application, rapidity when dealing with large numbers of cases, early cleaning of wounds and abatement of constitutional reaction to absorption, flavine (and its congener brilliant green) is an admirable application under all circumstances, but especially when surgeons are few, time is short, and wounds are many. No special technic is required, for after adequate previous surgical treatment any dresser can fill the wound cavity with gauze dipped in 1 in 1000 solution of flavine. In none of the cases under observation has skin irritation been observed. It has been clinically apparent in a few cases only that there is a certain amount of surface destruction in the wounds. In these cases a fibrinous pellicle forms, perhaps due to the use of too concentrated solution. This pellicle is readily removed by the application of saline solution, and also it is found that the addition of hypertonic saline solution to the antiseptic is useful in producing free exudation. W. H. F. A.

Observations upon Prognosis of Irritable Heart of Soldiers.—LEWIS (*Lancet*, February 2, 1918) outlines some results of the method employed in sorting those soldiers for duty who have been admitted to hospital for cardiac disabilities. All soldiers admitted to the Military Heart Hospital are submitted to a full physical examination, and within the first few days of their stay all cases presenting unequivocal signs of mitral stenosis, aortic disease, aneurysm or material cardiac enlargement are recommended for discharge as permanently unfit. On the basis of former experience are now also eliminated those who give a clear history of repeated or recent attacks of rheumatic fever, who show very high rates of heart beating or complain of severe precordial pain accompanied by hyperalgesia. All are eliminated in whom a positive decision can be reached, none are eliminated in regard to whom a divergence of opinion may exist. The whole remainder is submitted to graduated exercises and marches, and the reactions to these exercises form the chief basis

upon which the military prognosis eventually relies. The system has been in operation for two years, and during this period about 3000 patients have been studied, the average stay in hospital being between two and two and a half months. Between May and November, 1916, some 558 cases, who had successfully passed the preliminary examination intended to eliminate the obviously diseased, were discharged from hospital. It is with this group of men, especially the consideration of their after-histories, that the present report deals. Of this group of 558 men 286 were regarded as permanently unfit or placed in the sedentary class and the remaining 272 were classified for duty. Of these 86 have passed overseas within shorter periods than eleven months. A further number, 30, were in provisional units by the end of this period. Of the men going overseas it is estimated that more than half reach the firing line. These figures may be taken as representative for invalid soldiers suffering from so-called "irritable heart" and treated and sorted by a system of graded exercises. Lewis concludes from these analyses of after-history that the method has been highly successful, and urges its applicability to all convalescents from acute and subacute illnesses, medical and surgical. It is especially useful in reaching a decision as to health or unhealth in soldiers occupying the borderland between health and disease. The method is fully described in the recent Special Report Series, No. 8, of the Medical Research Committee's Report.

W. H. F. A.

REVIEWS

MODERN UROLOGY. By HUGH CABOT, M.D., F.A.C.S., Chief of the Genito-urinary Department of the Massachusetts General Hospital. Two volumes. Pp. 1452; 632 engravings and 17 plates. Philadelphia and New York: Lea & Febiger, 1918.

THE well-known editor of this work, consisting of two volumes, comprising the composite authorship of twenty-nine men identified with urology, has placed before the profession a treatise which must occupy a foremost place among the modern books on this subject. One is reminded of Morrow's great *System of Genito-urinary Diseases, Syphilis and Dermatology*, or Frisch and Zuckerkandl's peerless classic of three volumes on the subject of *Urologie*. It is not true, as the editor alleges, that none of the surgeons contributing to Morrow's *System* were specialists; moreover, it is a fact that a number of the contributors to the present volume, namely, Baer, Squier, Lower and Buerger, are general surgeons. Certainly this additional experience in nowise detracts from their reputations as urologists qualified to write authoritatively. The editor's avowed intention has been to give articulate expression to American urology. It might be questioned whether eighteen-twenty-ninths of this resides in Boston and New York.

Cabot himself recognizes the inherent weakness of composite authorship leading to a work of two volumes. This is specially pertinent in realization that in such a treatise syphilis has been divorced, except in so far as it concerns the genito-urinary apparatus. As a text-book for students, any two-volume work necessarily is destined to lose popularity comparatively with a single volume. On the other hand, irrespective of the conflict of opinion, duplication of matter, as evidenced in the chapter on diseases of the urethra in the female, in which the consideration of gonorrhoea is largely a redundancy, in view of the foregoing treatise on gonorrhoea in the male, also the duplication of certain well-known engravings and a certain loss of balance tending to disjointedness, the work makes a strong appeal to both practitioners and specialists.

The first volume opens with an historical sketch of genito-urinary surgery in America, which is most interesting and instructive. The cystoscope and its use by Buerger is a classic. Chapters on methods of diagnosis, roentgenology, and syphilis of the genito-urinary organs are followed by sections devoted to the penis,

urethra, scrotum, testicles, prostate, and seminal vesicles. The second volume is limited exclusively to the diseases of the bladder, ureter, and kidney.

Great credit is due the editor for so well balancing and proportioning the component chapters of the work. The chapters on obstruction and cancer of the prostate, urinary calculus and malformations of the bladder are exceptionally commendable. In the chapter on bladder tumors the reviewer takes exception to the term "malignant papilloma," and believes that when a papilloma becomes malignant it ceases to be a papilloma and becomes a carcinoma. Likewise, the term "unipolar" should be discarded in conjunction with electric currents; there is no such thing. In the same chapter there appears a disproportion in the number of illustrations as to treatment and pathology. Likewise the chapters on diseases of the penis and stricture of the urethra are strikingly devoid of illustrations. Exception must also be taken to the advocacy of "spinal anesthesia with tropacocain (1 c.c. of 5 per cent. solution) in preference to general anesthesia as an efficient and useful means for making an examination of the female urethra or for treatment of urethral conditions in cases impossible to examine under local anesthesia."

The consideration of and space devoted to the fourth venereal disease, "erosive and dangerous balanitis," is very timely and commendable and could not have been better or more authoritatively presented.

The reader is frequently impressed by quotations *in extenso* of authorities when he would prefer to learn the writer's own experience. It might be argued that inadequate consideration is given to the organic and inorganic constituents of the urine in health and disease or that the work would be enhanced by a chapter on nephritis. Few urologists still attribute much of a role to tonsillitis as a cause of ureteral stricture. Again, the critic must take exception to the statement relative to indigo-carmin as a functional kidney test that "for accurate estimation of renal function its position has been superseded." Partiality is obviously evident when three times the space is given to phenolsulphonephthalein as to all other functional kidney tests of elimination. We must also deplore the teaching or necessity of ureteral catheterization of the supposedly normal kidney for diagnosis and the best treatment of renal tuberculosis. Recourse to the use of some functional kidney test not dependent upon ureteral catheterization—as indigo-carmin by the method of chromo-ureteroscopy—would almost invariably obviate the necessity of resort to "operation for purposes of diagnosis" in difficult cases of descending urological or renal tuberculosis.

The merits of Cabot's *Modern Urology* so far transcend its demerits that detailed criticism would appear to be hypercritical and unjustifiable. The work is an enviable achievement, and is

destined to be a perennial monument to the expert professional attainments of its editor and collaborators. The character of the printing and illustrations, the quality of the paper employed and the excellent binding are merely additional evidences of the customary high-class work of the publishers. P. A. T.

THE PRINCIPLES OF HYGIENE. A PRACTICAL MANUAL FOR STUDENTS, PHYSICIANS AND HEALTH OFFICERS. By D. H. BORGEGY, A.M., M.D., D.P.H., Associate Professor of Hygiene and Bacteriology, University of Pennsylvania. Sixth edition. Pp. 543. W. B. Saunders Company, 1918.

As the author states, this book has been prepared to meet the needs of students of medicine, public health officers and students in architecture in comprehending the principles on which modern hygienic practices are based and also the sanitary requisites in ventilation, heating, water supply and sewage disposal. No one is better qualified to write on these subjects than Dr. Borgegy. The material is handled in his usual concise manner, which adds so greatly to the value of the book. However, the progress in the application of the principles of hygiene is so rapid, both in civil and army life, that it is difficult to keep pace in these days of our great war, so that even between editing and publication of such a treatise many new applications are presented.

The first six chapters of the present edition cover air, ventilation, heating water, sewage and garbage disposal. Then follows a long chapter on food and dieting, surprisingly well covered in such a space. A chapter on exercise is excellent. Next is discussed clothing and personal hygiene, and the usual points are brought out. The chapter on industrial hygiene is altogether too short and in nowise adequately covers this most important, if not the most important, field for the practical application of the principles of hygiene. Comprehensive mortality tables are given for the various trades, and some mention is made of the causes of this mortality. Little is said, however, of the effect of the several industries upon women as compared with men, and nothing at all on the effect on the birth-rate or the health of the children of working mothers.

The chapter on school hygiene contains a fund of information and chapters on military and naval hygiene are full; but of course there will be much more to be said on these two phases of the subject after the war is over.

Chapters on soil and habitation follow, and then two chapters on the vital causes of disease and on disinfection. It is easy to appreciate that these two chapters are written by an authority on the subject. The volume ends with chapters on quarantine, quarantine regulations and vital statistics. C. N. S.

APPLIED BACTERIOLOGY. By C. H. BROWNING, M.D., D.P.H.,
Director of the Bland-Sutton Institute of Pathology, Middlesex
Hospital. Pp. 291. London: Henry Frowde and Hodder &
Stoughton, 1918.

ONE of the most interesting and important recent developments in bacteriology concerns the properties of certain antiseptics and their use in the isolation of bacteria, especially the value of brilliant green and telluric acid in fluid medium in the isolation of typhoid-paratyphoid bacilli from feces in the diagnosis of intestinal infections or "enterica" as they are now comprehensively termed. This little book presents an excellent review of the researches of the author and his colleagues in this important field, together with a review of the more important papers by others on this subject, so that conclusions are based upon the work of trained and critical independent observers. Chapters are also devoted to the isolation of *Bacillus diphtheriae* and diphtheroids by means of a simple medium containing telluric acid; the selective action of thallium acetate and thorium nitrate upon *Bacillus pyocyaneus* and organisms of proteus type and ultra-violet rays upon *Bacillus coli communis*, *Bacillus typhosus*, meningococcus and acid-fast bacilli; the chemistry and practical application of certain antibody reactions are briefly considered, with special reference to the aid they give in the diagnosis and differentiation of bacterial species, and the book ends with a brief chapter upon the clinical and bacteriological aspects of tetanus, based mainly upon recent experiences with this infection in the present war.

The title of the book leads one to expect a wider discussion of the practical applications of bacteriology, but in its limited scope the subject matter is presented in an excellent manner and should prove of much value to laboratory workers and also to those concerned with the clinical and administrative aspects of medicine, especially those engaged in army and municipal work. J. A. K.

SURGICAL CLINICS OF CHICAGO, VOL. II, No. 1 (FEBRUARY, 1918).

By NUMEROUS AUTHORS. Pp. 226; 73 illustrations. Philadelphia and London: W. B. Saunders Company, 1918.

THE reputation of the preceding numbers of this publication is maintained by this one. The subjects range from the common interesting conditions, like duodenal ulcer treated by Andrews, to those which are rare and interesting, like gall-stone ileus, discussed by Bevan. Between these extremes we have a large list of surgical affections and operations handled by competent Chicago surgeons,

as a rule, with lucidity and brevity. For examples, we have radium in gynecology by Watkins; urethral strictures by Eisendrath; arthroplasty by Hessert; conservative surgery in children by Carl Beck; a large group of orthopedic cases by Parker and osteoarthritis by Ridlon. The variety in the method of presentation of the wide range of conditions helps to maintain the deserved popularity of this surgical journal.

T. T. T.

HAND-BOOK OF OPERATIVE SURGERY. By WILLIAM IRELAND DE C. WHEELER, Lieut.-Col., R. A. M. C., Surgeon to Mercer's Hospital. Third edition. Pp. 355; 226 illustrations. New York: William Wood & Co., 1918.

THIS small volume, as its title indicates, is devoted to the common surgical operations, particularly of civil life. Ligations and amputations fill one-third of the book. Local anesthesia, direct transfusion of blood, the common deformities of the legs and feet, tendon transplantation and bone-grafting are briefly considered. An attempt is made to provide an introduction to the type of operation confronting the inexperienced practitioner in military and civil hospitals. It is an excellent book for the field it aims to supply.

T. T. T.

MANUAL OF SPLINTS AND APPLIANCES FOR THE MEDICAL DEPARTMENT OF THE UNITED STATES ARMY, 1917. Pp. 208; 173 illustrations. New York: Oxford University Press.

A BOARD of medical officers was appointed for the purpose of standardizing certain medical department supplies. The best guarantee of the character of the work is the board itself: Lieut.-Col. William L. Kellar, M. C.; Major Robert B. Osgood, M. R. C.; Major Alexander Lambert, M. R. C.; Major Joseph A. Blake, M. R. C.; Captain W. S. Baer, M. R. C., and Captain Nathaniel Allison, M. R. C. This manual does not aim to be a complete treatise but to put into the hands of the military surgeon a practical time-saving guide, in which the text-book has been subservient to graphic illustration.

T. T. T.

PROGRESS OF MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Treatment of Gunshot Wounds of the Knee-joint.—PAGE (*British Med. Jour.*, September 1, 1917, 282) bases his study upon an analysis of 70 cases submitted to operation. Thus all cases with clean perforating wounds remaining clean coming under observation in the same period are omitted. There was articular bone injury in 59, the missile lodged in 51, recovery occurred without obvious infection of the joint in 45, amputations were done in 10, the deaths occurring after amputation were 4, and the total deaths 5. In dealing with wounds of the knee-joint the natural defensive powers of the part against infection should be borne in mind. To obtain fair play for the defense should be the aim of the surgical procedures adopted. Primary prophylactic (that is within twenty-four hours of injury) operations should be radical, and secondary operations undertaken on account of progressing infection, should, short of amputation, be planned on conservative lines. The expectant treatment of wounds of the knee-joint is only justifiable in the case of typical perforating injuries due to a rifle bullet. All wounds of the joint caused by shell fragments or distorted bullets should be considered as primarily infected. The primary prophylactic treatment should consist in the removal of any foreign bodies present and in the excision of the whole wound tract at the earliest possible time after injury. Any delay beyond twenty-four hours will entail failure in a certain proportion of cases. The results at present are particularly bad in cases in which gross comminution of the diaphysis is present. A primary excision or erosion of the joint (within twenty-four hours) would probably improve the results in such instances by preventing the development of entomyelitis. Repeated aspiration of the joint and the intra-articular injection of any of the antiseptics in use are calculated to prejudice the natural defense. It is safest to leave some drainage along the wound tract after operation for a few days, certainly when bone injury is present. Any infection then left may

become localized in the same way as occurs in the case of the peritoneum. A gauze wick makes a satisfactory form of drain. Immobilization of the joint during all critical periods is essential. An interrupted plaster-of-Paris splint affords the best means of effecting this. When general infection of the joint has taken place, treatment by fixation, lateral arthrotomy, and immunization gives the best chance of saving the limb, secondary abscesses are to be expected and should be evacuated after their complete development. Neither cross-section and flexion of the joint nor secondary excision of the knee are sound procedures.

Injuries to the Peripheral Nerves and Their Treatment.—MOYNIHAN (*Surg., Gynec. and Obst.*, 1917, xxv, 595) says that the earliest examination should be made of all wounds in which division of a nerve trunk is probable. If at the casualty clearing station such a lesion is found, end-to-end sutures should be adopted forthwith. This is most likely to be possible in cases in which primary suture of the wound, after excision, is found practicable. If secondary suture of the wounds, after the Carrel-Dakin method has been employed, is to be undertaken the union of divided nerves should be secured at the same time. If these methods have been attempted and have failed they do not prejudice the later union of the nerve. On the contrary, they probably ensure that an easier and more satisfactory operation can then be practised. Throughout the whole period before late nerve suture is attempted the strictest attention must be paid to the relaxation and nutrition of all paralyzed muscles, to the maintenance of suppleness in all joints moved by these muscles and to the preservation of the integrity of the skin. Operations upon nerve trunks demand the most scrupulous observance of the ritual of asepsis. There must be the greatest gentleness of manipulation; the nerve must not be injured by instruments or by the surgeon's finger; it must not be separated from its sheath or disturbed overmuch from its bed; it must not be chilled or allowed to dry. All sutures must be of fine catgut and introduced with most punctilious accuracy. Axial rotation of the nerve must be avoided. The cut ends of the nerve before approximation must show clearly the fibers of which the trunk consists. Nerve-grafting is of little or no value; nerve anastomosis is to be sharply condemned; the turning down of flaps from the nerve to bridge a gap is useless. Tendon transplantation is of great value when nerve suture is impossible or when suture has given a result not entirely satisfactory.

Gunshot Wounds of the Lungs and Pleura.—MOYNIHAN (*Surg., Gynec. and Obst.*, 1917, xxv, 605) says that the approximate mortality from gunshot wounds of the chest at all parts of the line of communication is 20 per cent. The causes of death are hemorrhage, as a rule, within twenty-eight hours, and sepsis after the third or fourth day. The local conditions in wounds of the chest wall and lung are in all respects similar to those met with in wounds elsewhere. The missiles are the same, their destructive effects upon the tissues are the same, and the infecting organisms are the same. The lung tissue is more resistant to attack than many other tissues. The opening of the pleural cavity and the resulting exposure of a large serous sac to infection and all its consequences add, however, a danger of the most threatening character. The chief essential in the treatment of all cases of penetrat-

ing wound of the chest is rest. In clean, perforating wounds of the chest, rest, together with the cleansing and dressing of the wound of entrance or exit, will lead to the recovery of the great majority of cases. In cases of "open thorax" the earliest and most complete effort possible must be made to secure closure of the wound after an appropriate toilette. In those rare cases of grave hemorrhage when hemoptysis is present or when the blood escapes by the wound a direct access to the source of the bleeding must be obtained, when all contingent circumstances permit, and the wound in the lung must be treated by suture, preferably, or by plugging of the cavity from which the blood escapes. In cases of hemothorax, when the blood effused is small in quantity and remains sterile, no active measures are necessary unless absorption is long delayed. Aspiration, repeated if necessary, may then be performed. In cases of hemothorax, when the blood effused is large in quantity and sterile, aspiration after the seventh or eighth day, or earlier in cases of urgent dyspnea, certainly hastens convalescence, permits a more rapid expansion of the lung, and prevents the formation of adhesions which may permanently cripple the free movements of the lung. In cases of hemothorax whether the amount of blood is small or large, when infection takes place, open operation is necessary. Early operation, both when the Carrel-Dakin technic or Morison method are adopted, saves many weeks of convalescence and permits of a more perfect functional recovery. Small foreign bodies, or rifle bullets, embedded in the lung, often cause no symptoms; they become encapsulated and may safely be left. Larger foreign bodies retained in the lung may cause distressing or disabling symptoms for long periods. In such cases removal after resection or elevation of the fourth rib through an anterior incision will allow of the safe removal of the projectile from any part of the lung. Pieces of metal so removed are almost always infected.

Gunshot Wounds and Their Treatment.—MOYNIHAN (*Surg., Gynec. and Obst.*, 1917, xxv, 583) says that perfect mechanical cleansing, that is, the excision of all contaminated, infected or dead parts, the removal of all fragments of clothing (by far the most important of all causes of continuing infection in a wound) and of all projectiles, is the supreme necessity in all cases. In early cases this may allow of immediate closure of the wound, which will be followed by healing in the great majority of cases, say in 80 per cent. or perhaps even in 90 per cent., of those in which there is no loss of tissue. In infected early cases the mechanical exposure and cleansing may be followed by a treatment directed to the removal of the remaining infection. Physiological and antiseptic methods have each their advocates. The aim of both is to permit of the earliest prudent secondary closure of the wound. In infected late cases a thorough mechanical exposure and cleansing of the wound and the parts around will allow of secondary closure forthwith if certain antiseptic pastes are used. Experience shows that similar results have followed upon this mechanical treatment of the wound without the introduction of antiseptics. A further trial in this class of cases may show that the natural defences of the tissues are ample to deal with the infections then remaining. It is the natural defensive powers of the body fluids and tissues, of serum and leuko-

cytes, that are the chief agents in finally subduing the bacterial infection in a wound. Sufficient reliance does not appear to be placed upon the stupendous power the body tissues possess for controlling infection. Finally, full emphasis must be laid on the paramount necessity for the complete immobility of wounded parts at all times and on all occasions. So will one of the most powerful agencies making for reinfection and auto-inoculation be kept in check.

Urinary Extravasation.—WOLFER (*Surg., Gynec. and Obst.*, 1918, xxvi, 296) after a careful study of some 12 cases under his own care and 31 cases obtained from the records of the Cook County Hospital of Chicago, emphasizes the following points: Extravasation of clean urine may present few signs early and not produce marked reaction for a long period of time, up to two or four weeks, and then rapidly destroy life by sepsis. Urine in the presence of a stenosis of the urinary outlet is usually septic. Many cases of urinary extravasation are caused by a rupture of the urethra due to an inflammatory process, which can be detected before perforation. Urinary extravasation must be treated according to the condition of the urine. In clean urine cases, closure of the opening with drainage in cases of necrosis is the method of treatment. In septic cases, suprapubic cystostomy, with wide incisions in all infiltrated and edematous areas, rest to the urethra, and subsequent careful dilatation of the strictures, is the only safe method of procedure.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Alkali Reserve in the Blood of Pellagrins.—A study of a series of 36 pellagrins, in various stages of the disease, leads JOBLING and MAXWELL (*Jour. Am. Med. Assn.*, 1917, lxi, 2026) to conclude that the alkali reserve of the blood in pellagra does not vary from the normal in either the acute or the chronic cases; therefore there is no acidosis or alkalosis in pellagra. The viscosity of the blood shows a slight decrease from normal.

Stimulation of the Respiration by Sodium Cyanide and its Clinical Application.—In a large series of animal experiments LOEVENHART and others (*Arch. Int. Med.*, 1918, xxi, 109) found that the intravenous injection of sodium cyanide caused a profound but fleeting stimulation of the respiratory center; that the continuous intravenous infusion produced a continued stimulation of the center; that the factor of safety was large, the effective dose being only about one-twentieth of the toxic.

The very marked improvement in respiration and the absence of untoward effects in animals suggested to the authors that the use of cyanides against threatened respiratory failure in man should be revived. The dispute into which the cyanides have fallen is due, they believe, to their fleeting action, the uncertainty of absorption when administered by mouth, the instability of the preparations used and the popular but erroneous idea that the cyanides are very poisonous. The first and second of these objections were overcome by the continuous intravenous injection of the drug; the third, by using chemically pure sodium cyanide; and the last by observing the effect on the respiration, the slightest excess causing a depression which disappeared as soon as the injection was stopped. The writer and his co-workers treated 10 patients, whose death from respiratory failure seemed imminent, with the intravenous injection of fiftieth-normal sodium cyanide solution. In some patients the treatment was repeated, so that the present report comprises fifteen treatments. In every case a marked stimulation of respiration was obtained, beginning about twenty seconds after starting the injection. The degree of stimulation could be accurately controlled by the rate of injection. The duration of the stimulation following a single injection rarely exceeded thirty seconds and depended on the size of the dose and on the rate of injection. The dosage required to produce a therapeutic effect in man varied in different cases and according to the condition of the patient. When large respiratory movements are desired, as in resuscitation from drowning, a single injection of 5 c.c. may be employed; when it is desired to produce a milder but continuous stimulation of the respiration the fiftieth-normal sodium cyanide solution should be injected continuously at a rate varying from 1 c.c. in thirty seconds to 1 c.c. in fifteen seconds. By watching the injection there is no difficulty in deciding the proper rate for a given case. The injection should be slowed or stopped temporarily when any of the following symptoms appear: marked pallor, nausea, marked increase in pulse rate (30 per cent), depression of the respiration and any other untoward symptoms. In the opinion of the authors the intravenous injection of sodium cyanide should prove useful in the following conditions: depression of respiration resulting from increased intracranial pressure, however produced, until the condition can be relieved by decompression; resuscitation from drowning; embarrassment of the respiration under any form of anesthesia, and other forms of respiratory depression, when it may be given in conjunction with artificial respiration.

The Action of Tyramin on the Circulation of Man. — HEWLETT (*Arch. Int. Med.*, 1918, xxi, 411) summarizes the changes observed in 28 individuals after the subcutaneous injection of from 40 to 80 mg. of tyramin as follows: An increase in the systolic blood-pressure, the pulse-pressure and the volume pulse in the arm; a slowing of the heart rate, apparently as the result of vagus stimulation by the heightened blood-pressure and an increase in the size of the T-wave in the electrocardiogram, with the occasional occurrence of premature contractions. The maximum effect on systolic blood-pressure was usually attained within ten minutes of the injection, the return to normal occurring within twenty to thirty minutes. The rise in diastolic pressure was slight compared with that of the systolic, so that the pulse-pressure was

markedly increased. The vascular sounds heard during the auscultatory determination of blood-pressure were much louder at the height of the tyramin action. In animals tyramin has been demonstrated to possess a vasoconstrictor action, but Hewlett's observations point to an increased cardiac output rather than to a vascular effect, comparable, for instance, to that produced by pituitary extract. Hewlett believes the increase in pulse-pressure to be due mainly to the increased output of blood with each ventricular systole and not to a constriction of the bloodvessels, as in that case one would expect to find a far greater rise in the diastolic pressure than that actually observed. Moreover, the increase in arm pulse volume is not typical of vascular constriction, and is more readily explained on the assumption of an increased cardiac output. The total output of the heart per unit of time (considered as the produce of heart rate times pulse-pressure) was materially increased (50 to 100 per cent.) by tyramin. The subcutaneous injection of epinephrin for purposes of comparison was found to produce an apparent increase in cardiac output, an increase in pulse-pressure and some increase in pulse rate. As there is a close connection between ventricular fibrillation and very numerous ventricular premature contractions, and it seems possible that under proper conditions tyramin might cause a dangerous or even fatal ventricular fibrillation in man, Hewlett urges caution in the use of this drug if premature contractions are present or if there is any reason to suspect a condition of increased irritability in the heart muscle, such as seems to occur during chloroform anesthesia.

Pharmacodynamic Examination of the Vegetative Nervous System in Typhoid Fever.—This paper by MATSUO and MURAKAMI (*Arch. Int. Med.*, 1918, xxi, 399) is the result of a pharmacodynamic investigation into the condition of the vegetative nervous system in 46 cases of typhoid fever and paratyphoid B. Atropin, epinephrin and pilocarpin were injected subcutaneously in turn at intervals of from one to two days. The doses of atropin (0.001 gm.) and epinephrin (0.001 gm.) were the same as those used by Eppinger and Hess. No glucose was given, as in the original method of Eppinger and Hess, but glycosuria was qualitatively tested for. The observations were all made between the first and third weeks of the disease. The reactions observed were considered as positive under the following conditions: Atropin, 0.001 gm. When the pulse rate was increased by more than twenty beats per minute. An increase of less than twenty beats when accompanied by increased thirst or palpitation was considered positive. Epinephrin, 0.001 gm. An increase in pulse rate of more than twenty beats per minute, a rise in blood-pressure of over 20 mm. Hg., marked tremor, palpitation and glycosuria (no previous administration of glucose). An increase in the heart rate alone, unless marked, was considered negative, while glycosuria unaccompanied by other symptoms was classed as positive. Pilocarpin, 0.007 gm. Sweating and salivation alone, unless very pronounced, were not considered as positive; when accompanied by gastrointestinal symptoms the reaction was classed as positive. A summary of the findings of Matsuo and Murakami shows that of the 38 cases of typhoid fever, 14 cases corresponded to vagotonia, 11 cases corresponded to sympathicotonia, 3 cases were sensitive to all three drugs, 7 cases

were sensitive to pilocarpin and epinephrin and 3 cases were sensitive only to pilocarpin. The 5 fatal cases in this series all showed sympathicotonia, and the authors suggest that this fact may serve as a basis for establishing prognosis in typhoid fever. They consider the prognosis bad in cases of bradycardia insensitive to atropin and pilocarpin and sensitive to epinephrin. These authors found youth more sensitive than age to atropin, but no relation between age and sensitivity to pilocarpin or epinephrin.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Prophylaxis of Infection in Nurseries.—BARBIER (*Arch. de méd. des enfants*) describes the precautions taken in the Hérold Hospital, in Paris, to prevent contagion among infants. The nurses wear a veil like those worn in the operating room, and only well-trained and experienced nurses are placed on duty in these wards. Under the heads of the infants are put sterile folded cloths which greatly lessen the infections developing upon the head. One nurse has charge of the food for all of the infants, written directions being given in each case. She collects the directions and prepares the food in a room apart from the ward. The bottles are kept in wire baskets, each of which is marked with the number of the bed, and the bottles are prepared at 11 A.M. for the twenty-four hours. Infants unable to take cows' milk have done well on ass's milk when breast feeding could not be obtained. From 1909 to 1913 the mortality among 1238 infants was 35 per cent., and 29.5 per cent. of the 442 deaths were from typical tuberculosis confirmed by autopsy. There were 311 marasmic infants, among whom there were 141 deaths, and of these 62 per cent. were from septicemia, only 15.1 per cent. actually dying from marasmus. Of the infants having septicemia 70 per cent. were under six months, and in many of these hospital contagion was responsible. It is essential that each child have a separate crib and that infants already infected should be kept entirely away from others and their nurses also. As the infants grew better it was desirable to take them away from the hospital at the earliest possible moment. There were 46 cases of typhoid, none of which terminated fatally, and this is ascribed in large part to the fact that they were given no milk.

Labor Obstructed by a Contraction Ring.—WHITE (*British Medical Journal*) reported, in 1912, 3 cases in which labor was obstructed by a contraction ring. His attention was called to this condition by the examination of a uterus removed during labor by hysterectomy. This specimen showed that the contraction formed from a depression in the child's body and that the part below the ring was

not pathologically thin. Thus the ring had no connection with the ring of Bandel, commonly called a retraction ring. The case now reported is that of a primipara in labor with whom a doctor had attempted to hasten delivery by manual dilatation of the cervix and the use of the high forceps and had failed. She had been in labor forty-eight hours. On admission, the head was in the cavity of the pelvis, the child was dead and in left occipitoposterior position. It was decided to wait for uterine contractions and perform craniotomy. When the fundus occasionally contracted, the head was perforated and with great difficulty extracted from the vulva with the cranioclast but the shoulders could not be delivered, even after cleidotomy and the fundus of the uterus became tetanic. As the patient passed into shock, a 7-pound weight was tied to the cranioclast and the patient was stimulated by transfusion and external heat for between one and two hours. Delivery was then easily effected by bringing the arms down over the head and making light traction. The fundus was flaccid and the placenta temporarily retained; this was removed manually, and an intra-uterine douch was given. The mother recovered, but there was considerable sloughing of the vagina, resulting in the formation of a fistula between the vagina and urethra and ureter. His fifth case was a multipara admitted in labor with a dead child and an offensive discharge from the uterus. There was a very tight contraction ring around the thigh of the child which did not yield to pressure. The mother being infected, the entire pregnant uterus was excised. She made an uneventful recovery.

Hydatidiform Mole and Chorio-epithelioma.—CATURANI (*Am. Jour. Obst.*, April, 1917) reviews the literature of this subject and reproduces illustrations of these two conditions. He believes that our inability to determine the future course of a hydatid mole depends upon the fact that it is very difficult to secure evidence of the actual invasion of the uterus. Could we observe that, we could form a much better idea as to the outcome of the case. When a mole is present in the uterus, the wall of the womb is softened and friable, and the tissues cannot be completely removed by a curette; probably the most reliable and efficient method consists in vaginal hysterotomy, and when this operation is done, one cannot only secure the remnants of the mole, but also a small section of uterine tissue to study the question of the invasion of the wall of the womb. When an hydatid mole attacks the tissues of the vagina this could not be considered a benign process. It is different from the deportation of villi in normal pregnancy. In hydatid mole the tissues grow abnormally and rapidly develop a tumor. Considerable time may elapse between the first appearance of metastasis in the vagina and its development to a serious nature, but if such metastasis has followed an hydatid mole, there is no question regarding its malignancy. If in a suspicious case the core of the villus is present, this does not exclude the possibility of malignant change, especially if the cells of Langhans are present in large quantity. These cells are almost pathognomonic of malignancy. Should a chorionic tumor be recognized, it should be considered as malignant without hesitation. In examining the tissues of a mole, if the essentials of the primitive chorion are present and growth is taking place, the

tumor is suspicious. To positively estimate its malignancy one must study the mole in relation with the surrounding maternal structures. Where the tissues show a tendency to penetrate the uterine wall, it must be considered a chorio-epithelioma. Marchand's classification of two types, syncytioma and chorio-epithelioma, is supported by statistics from clinical observation, and agrees with the anatomical constitution of the chorionic tumors. Seven cases have come under the observation of the writer and 6 of these are reported in brief: The first occurred in a woman, aged twenty-six years, following a normal confinement at term, and vaginal tumor developing twenty-eight days after confinement. In this tumor syncytial and Langhans's elements were both abundantly present. This patient died eight months after confinement. The second case followed an hydatid mole and in this case the syncytium predominated. This patient had been ill for many months and had been curetted three times before coming under observation. The tumor had almost entirely destroyed the posterior wall of the uterus which was about to rupture. Marked saprophytic infection was present. The uterus was removed, and eight years after the operation the patient is living and well. The third patient, aged forty-three years, had hemorrhage for fifteen months and had been curetted several times. On examining the uterus after its removal a wide tumor was implanted in the posterior wall toward the fundus. This was composed of syncytial elements. The patient died five months afterward with recurrence in the pelvis. The fourth case followed an hydatid mole at the fourth month with very rapid development. When seen, the patient was in such a condition that nothing could be done. The uterus was secured by autopsy and was studded with typical syncytial growths. The fifth case was a multipara who had severe hemorrhage for which she was curetted. She was thought to have had an incomplete abortion. Hemorrhage returned and curetting was repeated, and scrapings examined, showing transitional chorio-epithelioma. The uterus was removed for repeated hemorrhage. On examining the uterus, Langhans's cells and syncytial elements were in a state of necrosis. There was no trace of villi. The ultimate fate of this patient is not stated. The sixth case followed a normal confinement and was one of chorio-epithelioma. The uterus was curetted and a small vaginovulvar tumor was removed. The patient refused radical operation, and died six months after the confinement.

Shall the Curette Be Used in Cases of Infection?—POLAK (*Am. Jour. Obst.*, March, 1917) states that in treating cases of infection following abortion one must consider the period of gestation, the condition of the cervix, the amount of hemorrhage, and the presence or absence of sepsis. In clean cases after securing free dilatation of the cervix, complete evacuation of the uterus by the curette, forceps, and finger, with a strict, septic, surgical technic and the firm retraction of the uterus, leaves the woman in the best possible condition. If, however, she has had gonorrhoeal endocervicitis at the time of abortion she is practically infected. The majority of abortions, however, as seen in practice are not clean, because they have been examined or tamponed without surgical cleanliness of the vulva. So frequently does infection

follow manipulation under these circumstances that the custom has recently obtained of letting the uterus entirely alone in all suspected cases. The results were that patients did much better than formerly. In following up these cases it has been found that these patients had menorrhagia, sometimes very severely, for several periods after their discharge from the hospital. Recently cases have been divided into those in which abortion was begun and completed in the hospital under the most careful asepsis, and those which began outside of hospital and had been examined or packed one or more times without proper preparation of the external parts. These later cases are considered infected. Unless hemorrhage is severe these patients are treated in the Fowler position, with an ice-bag placed over the uterus. If there is considerable bleeding a sterile vaginal gauze tampon is firmly packed against the cervix. After this method of treatment the patients had prolonged menstruation and increased quantity of blood lost. In view of these facts, when a case is admitted bleeding, a very thorough antiseptic preparation of the external parts and vagina is made, the interior of the uterus is explored, and a culture made. If this is negative the uterine content is carefully evacuated after giving, by hypodermic injection, an ampoule of pituitrin. The emptying of the uterus is done by the curette or placental forceps when pregnancy is eight weeks or under, and with the placental forceps and fingers when it is past that time. Following the emptying of the uterine contents the interior of the uterus is iodized by packing with gauze soaked with tincture of iodine, and this pack is allowed to remain for twenty minutes. The routine culture of the interior of the uterus has shown that more than 61 per cent. have a pure culture of either staphylococcus or streptococcus when such culture has been made from forty-eight hours to four days after the supposed abortion. This explains why incomplete abortion, formerly subjected to routine curetting, has subsequently developed exudate in the perimetrium. When culture showed the presence of bacteria in the uterus the expectant plan of treatment was followed until a culture from the interior of the uterus showed no organism to be present, and then the cavity of the womb was curetted and carefully iodized. This was done not only to lessen blood loss at subsequent periods but to avoid leaving adherent tissue that might favor the development of chorio-epithelioma.

Hematocolpos in a Woman Aged Seventy-four.—GELLHORN, (*Surg., Gynec. and Obst.*, January, 1917) reports the case of a woman, aged seventy-four years, who had menstruated normally until thirty-five years previously. Then severe pain and obstruction to the discharge of urine lead to an examination. A large, fluctuating tumor was found filling the pelvis, extending upward almost to the umbilicus. The atresia of the senile period had entirely closed the vagina. Section was performed under spinal anesthesia and an enormous distention of the uterus and tubes with blood was found. The entire uterus was then removed and the tumor, which was connected with the vagina by loose connective tissue only, was removed unopened. The patient died from embolism on the fifteenth day. The cause of the bleeding was adenocarcinoma of the body of the uterus.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Radium in Uterine Cancer.—The experiences with radium in the treatment of uterine cancer at the Memorial Hospital in New York have been presented by BAILEY (*Surg., Gynec. and Obst.*, 1918, xxvi, 625), and he states that the recurrent cases showed the lowest percentage of improvement. The recurrence is usually behind the vaginal vault and the vagina itself is usually foreshortened and contracted. The primary cases are more amenable to the application of radium and the results are slightly better than when previous treatment had been instituted. Twenty-one per cent. of this class showed marked improvement with the possibility of remaining free from cancer. When a period of two years passes a fairly good estimate may be made as to ultimate results, and although not over 15 per cent. of the cases lived to that period, in those that did live the probabilities of complete retrogression are great. On the other hand, over 80 per cent. lived through the first six months, and it is very difficult to sift the good from the bad, for nearly all showed local improvement. Bailey is convinced that the inoperable cases do better without the preliminary Percy treatment, and he also believes that the initial dose of radium should be high and that it should seldom be repeated for the same area. Cross-firing should be made use of from within and from the surface of the body.

Radium in Uterine Hemorrhage.—The term uterine hemorrhage as employed by MILLER (*Surg., Gynec. and Obst.*, 1918, xxvi, 495) is limited to bleeding due to metropathies, disturbed ovarian function, chronic endometritis, metritis and fibroids of the uterus. Bleeding associated with syphilis, chronic liver and heart disease, lung and kidney affections, as well as the ordinary complications of pregnancy, is naturally eliminated and mentioned to emphasize the point that uterine bleeding is only a symptom and demands careful differentiation and accurate diagnosis in its management. Every gynecologist is impressed with the large number of cases of persistent bleeding that eventually require hysterectomy. If he is conscientious he can only regret keenly the necessity of performing a serious mutilating operation, especially when the pathologist reports little if any pathological change in the uterus. Radium has proved to be the long-sought specific in these cases, because of the simplicity of application, the short amount of time required to effect a cure and the uniformly satisfactory results obtained. The most plausible explanation of the action of radium in these cases is that it produces extensive structural changes in the endometrium. The author has had considerable experience along these lines and for the purpose of study has divided his cases into groups. The first group includes the cases commonly denoted as myopathia hemorrhagica (hemorrhage of the menopause). These cases, as a rule, present little

if any defined anatomical cause to account for the bleeding and comprise some of the most serious instances of acute hemorrhage. It occurs most commonly in women approaching the menopause, though it may be found in comparatively young women. The uterus may be normal in size or slightly enlarged, and often presents a normal endometrium. The bleeding is supposed to be due to a disproportion of connective tissue over muscular tissue in the myometrium or to some aberration of ovarian secretion or other ductless glands. In these cases the bleeding was controlled primarily in 100 per cent., with 90 per cent. of permanent results. The average time from the treatment until amenorrhea occurred was four weeks. The second group included patients presenting a history of menorrhagia or metrorrhagia, lasting for months or years, practically all of whom had a uniformly enlarged, hard or occasionally flabby, uterus. Many gave a history of puerperal complications. In some, the origin of the trouble appeared to be extensive lacerations of the cervix, involving the parametrium. These cases are ordinarily classified as chronic metritis, polypoid endometritis, hyperplasia, fibrosis, etc. Amenorrhea was produced in every case within one month after treatment, and all but two of the eighteen cases have recently been communicated with and none report a return of the bleeding. Many presented an enlarged uterus before the treatment, but every one examined three months or longer after the treatment showed a uterus approximately normal in size. The menopausal symptoms seemed to be more pronounced in this group than in any of the other series. The group of myomata comprises 26 cases, and in 22 cases the bleeding ceased within five weeks and has never returned. In 5 cases it was controlled for a few months, but was never so severe after its reappearance, while in 2 of these the menses became regular after eight months. In only 2 cases has the radium failed, and these would very probably have been relieved by another radiation. Control of bleeding is not the only desideratum in treating fibroid tumors; the growth of the tumor must be stopped and, if possible, the tumor be made to disappear. In 16 cases examined from three months to two and a half years after treatment there has been a reduction in the size of the tumor varying from complete disappearance in 3 cases to about one-half the original size in practically 50 per cent. of the number. Some further points in regard to the fibroid group are worthy of comment, namely, most of the growths selected for radium treatment were small, the only large tumors being those presenting contra-indications to operation. This feature is emphasized because Miller does not wish to imply that radium is to supplant surgery in the treatment of fibroids, but it is a most valuable adjunct to surgery. Two cases in this series illustrate conclusively that radium is more effective than the roentgen rays. Both had been given twenty exposures by an experienced roentgenologist, who employed the Gauss technic, with only temporary results. Only one intra-uterine application of radium sufficed to stop the bleeding permanently. In a fourth group the author records 2 cases of serious uterine bleeding in young girls who had been treated by rest, tonics, astringents, ovarian extract and curettage. The uterine scrapings apparently showed hyperplastic glandular endometritis. The application of small doses of radium produced results that were all that could be desired, even though the risk of permanent amenorrhea was greater than should be taken in the ordi-

nary case of this type. Both of these cases now menstruate regularly after a period of amenorrhea which lasted three months. While the results obtained by various authorities with the use of radium are practically the same, the dosage employed has been by no means standardized. It has been practically established that a 1000-milligram-hour exposure is almost certain to produce permanent cessation of the menses, but in the treatment of fibroids the size of the growth and the degree of hemorrhage should govern the amount used and the duration of the exposures. If the only annoyance a woman experiences who suffers from a fibroid is bleeding, is there sufficient justification for performing hysterectomy? To this question the author answers in the negative. If the growth is sufficiently large to produce pressure symptoms, operation is preferable because of the time consumed in reducing it by radium. If evidence of infection or degeneration exists or the appendages are diseased, operation is the best procedure. If the woman is young she should be advised to submit to operation with the idea of performing myomectomy and preserving the uterus. For small and medium-sized growths and those presenting contra-indications to operation, radium is the ideal remedial agent. Submucous growths should be treated surgically unless contra-indications to operation are present, owing to the tendency of this type to become infected or develop other degenerative changes.

End-results of Cystocele Operations.—The condition of the interior of the urinary bladder in patients who have had some sort of cystocele operation has been studied by BROWN and RAWLS (*Surg., Gynec. and Obst.*, 1918, xxvi, 502). In securing the end-results it was considered necessary that at least one year should have elapsed since operation before the examination of the bladder was performed. In all they examined about 50 patients cystoscopically, and with 1 exception none of the patients examined stated that any urinary symptoms they might have had were aggravated by the operation; to the contrary, the very large majority stated that they had been in part or entirely relieved of such symptoms. This fact is very striking, since only 9 of the 49 patients examined showed a normal bladder base. The character of the cystocele operations done upon these patients varied greatly, but in the larger number the operative procedure consisted in freeing the bladder from the vaginal mucosa and uterus, coapting the prevesical fascia under the bladder and approximating the vaginal mucosa after the excess had been removed. In a series of 8 patients the base of the bladder was found to be thrown into horizontal folds of varying degrees of prominence, but the kind of operation done did not seem to bear in a marked degree upon the character and extent of the permanent folds found to be present. As an end-result in all of the 8 patients under consideration in this group it was found that in 6 there were no urinary symptoms, while in the remaining 2 the urinary symptoms prior to the operation were improved. In another group of patients the folds of the base of the bladders were found to be from side to side (transverse), opposite to the direction of the folds of the bladder bases of those just reviewed. Here, again, the character and degree of the convolutions, as in the previous cases, did not bear any definite relation to the kind of operations done and, furthermore, no vesical irritation that was present

could be charged up to the operation. The final group of cases brought together are those on whom the uterus was interposed between the bladder and the vaginal layers, including 10 cases. As would be expected the bladder base was thrown into a large horizontal fold, with deep sulci on one or both sides and also frequently above the fold. Trigonitis, with the frequent presence of dilated capillaries throughout the entire bladder mucosa, was the rule. The vesical symptoms of the patients of this group were as with the patients of the previous groups, remarkably negative. Seven patients were free from any vesical irritation or frequent urination; with one the loss of control before the operation was not relieved. This detailed review of the study of the end-results on these patients, from the view-point of the anatomical condition in which the base of the bladder is left, is surely not of a flattering character. That the abnormal character of the conditions found were permanent cannot be questioned, since they did not disappear under full distention of the bladder as would have occurred if they were merely due to incomplete filling of the bladder at the time of the examination. The query naturally presents itself that although apparently there is no disturbance as a result of this departure from the normal plane-like floor, does not such a state render more possible some future disturbance of a systemic character? The truth of such a possibility cannot, from the nature of the condition, be determined except by painstaking investigation of each individual patient over a long period of years, and this is hardly possible on account of the nomadic character of the average hospital patient.

OPHTHALMOLOGY

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

DENVER, COLORADO,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,

PHILADELPHIA.

Traumatic Variations in the Tension of the Eyeball.—MAGITOT (*Ann. d'Oculist.*, January, 1918, 1) publishes a study of the tension of the globe as affected by traumatism, which may show itself either in hyper- or hypotension. He regards this as depending upon two principal causes: active and passive. The former depends upon mechanical interference of the venous circulation in the orbit, hence extra-ocular. This gives rise to hypertension and persists as long as the disturbance in the circulation continues. The latter is due to a traumatism acting upon the intra-ocular vasomotor nervous mechanism. Traumatism of too slight intensity to determine within the globe grave lesions of the membranes may, however, occasion remarkable alterations in the tension of the organ revealing itself as a disequilibrium which becomes sensible as greater or less to the tonometer. Usually the hyper- or hypo-

tension tends to recede and the globe to take up the tension of the healthy eye; but in some cases a veritable instability of tonus occurs which may show itself brusquely as considerable variations in the tonometric readings; finally, in other cases, the disturbance of equilibrium persists as hypo- or hypertension. These phenomena are analogous to the vascular instability which occurs in shock. They depend upon vasodilatation or vasoconstriction due to reflex action of the intra-ocular sympathetic center.

Tuberculin in Eye Diseases.—VERHEYDEN (*British Jour. Ophthalm.*, April, 1918, 223) makes a plea for the more frequent use of tuberculin in strumous eye affections involving the conjunctiva, cornea, iris, ciliary body, sclera, choroid and tuberculous paralysis of the third nerve. A number of cases are detailed in which this treatment was highly satisfactory. Concomitant treatment consisting of 4 per cent. solution of diosin and subconjunctival injections of saline solution are useful adjuvants. He concludes that many eyes will be saved by tuberculin which would formerly have been lost or greatly damaged. Carefully tested and manipulated, risks of accidents from tuberculin are negligible; the results will be most gratifying in confirming a doubtful diagnosis and in ameliorating or altogether curing these serious and rebellious diseases.

Iritis and Cyclitis in Dysentery.—MAXWELL and KIEP (*British Jour. Ophthalm.*, February, 1918, 71) observed 6 cases all from the Mediterranean area, the subjects of infection with *Bacillus dysenteriae* (Shiga), who developed iritis or cyclitis. They conclude that patients suffering from an infection by this bacillus may occasionally develop anterior uveitis as a result of this infection, as pointed out by Morax. The ocular infection may or may not be accompanied by articular manifestations. These affections would appear to occur most frequently about a month after the first signs of involvement of the bowel, but may occur as early as the twelfth day. The artculo-ocular syndrome corresponds exactly to that occurring in another infection of a mucous tract, viz., gonorrhoea, as pointed out by Garrod.

Close versus Distant Illumination for Operations.—MADDOX (*British Jour. Ophthalm.*, February, 1918, 84) has attached to conjunctival forceps for operations on after-cataract as well as for emergency night operations a tiny screened electric lamp to one limb of the forceps half an inch from the gripping end. This attachment can be made with adhesive strapping or, better still, by a very light metal clip or steel wire, into the curl of which an ordinary bulb from a child's flash lamp is so screwed as to illuminate the iris brilliantly, when the forceps are gripping the limbal conjunctiva. The connecting cord must be of a feather-weight character. The grip of the forceps ensures a perfectly steady light and maintains its distance from the cornea constant. It is for needling operations that the method is ideal, and it also greatly facilitates the removal of foreign bodies from the cornea. While distant lights have some advantages of their own, especially in large hospitals, some form of close illumination has certain advantages: these are greater economy, greater portability and greater kindness to the patient's eye. A close light is diffused widely over his retina, with no

possibility of the image of the filament being thrown thereon. It also increases the surgeon's visual acuity. The smallness of the patch of light on the patient's eye is less disturbing than a widespread reflection from the whole face and pillow.

Disinfection of Artificial Eyes.—COULOMB (*Ann. d'Oculist.*, April, 1918, 202) observes that while the method of choice is boiling it is extremely slow. The eye must not only remain in boiling water long enough, but to avoid cracking it is placed in cold water, the temperature of which is cautiously raised. After sterilization the water must be allowed to cool slowly and gradually to the room temperature. Placing a cold artificial eye in boiling water will invariably crack it. The author has experimented with new eyes, both double and single shells, and with pieces of old ones; the pieces were rubbed upon a carpet or on the ground. Immersion in various antiseptic solutions (bichloride of mercury, formol, etc.), failed to sterilize, as proved by the development of numerous colonies of different microbes upon culture media. In view of these negative results further experiments were made which led to the discovery that Gram's fluid (iodin 1, iodide of potash 2, water 300) furnishes a satisfactory solution; after immersion from five to ten minutes no colony developed in any of the tubes; in fact, when the time of immersion was reduced to as short an interval as seven seconds no colony was found to have developed five days later. It was also found that if the solution be diluted one-half it was still sufficiently strong for practical purposes. Tincture of iodine alone has the disadvantage that it stains the fingers and is much more difficult to wash entirely from the artificial eye—an inconvenience which does not belong to Gram's fluid, which is readily removed by rinsing in cyanide of mercury, 1 to 5000, or simply sterilized water. The experiments further showed that a new eye is more easily disinfected than an old one and that the double shells are more quickly sterilized than the single pieces. The above method is simple and entirely efficacious.

Simple Method of Recognizing Feigned Diplopia.—TERRIEN (*Arch. d'Ophthal.*, January-February, 1918, 45) recommends for the detection of simulated diplopia, placing successively a light blue glass immediately followed by an opaque one before the same eye, the subject under examination being in an ill-lighted room, and fixing a small flame. If he continues to complain of diplopia after the substitution of the opaque for the colored glass he is evidently simulating. Diplopia, as is well known, being frequently purely subjective of numerous simulated or exaggerated ocular affections, is one of the most difficult to recognize, particularly if it has actually existed for a time and the patient desires to prolong his period of disability. In slight cases the absence of limitation of movements of the globe and the integrity of the field of fixation render it impossible to exclude all possibility of diplopia and to assert positively simulation or exaggeration. Prisms, the diploscope or repeated examination with colored glasses may, from the discordances in the patient's assertions, determine the degree of sincerity; but frequently the data so obtained, even when there is no intention of simulation or exaggeration, in individuals not trained to observe, may leave the examiner in doubt. The advantages of a simple method like the above are obvious.

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

EMERITUS PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

Primary Mastoiditis, with Report of a Case.—SONNENSCHNEIN states (*Illinois Med. Jour.*, September, 1917) that the existence of a primary infection of the mastoid cavity has always been questioned, and the reported cases of this kind are rare in the literature of the subject, the assumption usually being that the mastoiditis is really secondary to a middle-ear inflammation, of fugitive character or minor evidence. In the case cited by the author the patient, a man, aged thirty-four years, with a negative history as to tuberculosis or syphilis, had complained of a pain in the left mastoid, especially at night, during three weeks preceding examinations. The left membrana tympani was practically normal on inspection, the left mastoid process somewhat tender; the hearing for unaccentuated whisper in the left ear was six meters, in the right ear seven meters. All tuning-forks were well heard in the left ear, and Weber was not lateralized. The pharyngeal mucosa was injected and the lymphoid tissue hypertrophied, and there was some tenderness and swelling of the left cervical lymph glands, but absolutely no involvement of the middle ear. For the relief of pain a carbolyzed glycerin pack was inserted in the canal, alcohol dressings were ordered for external use and internal medication included magnesium salicylate. For a period of two and a half weeks the patient was seen only occasionally, the pain varying in severity and at times almost disappearing. By the end of this time there was some desquamation of the left membrana tympani, but no other changes except a lessening of the hearing for the tuning-forks in the left ear. Ten days later the pains were very severe and a wide paracentesis was done without evidence of pus or other middle-ear secretion, but a few vesicles had appeared in the external canal. The Weber was now lateralized in the left ear. Two days later the patient was admitted to the hospital. The blood count showed 18,000 leukocytes; two days later there were 18,400 and two days later still 14,200. On admission to the hospital the temperature had a range of from subnormal to 101° F., and during the following week from subnormal to 102° F. Five days after admission there was swelling of the bony canal and the next day swelling over the left mastoid accompanied by a marked drop in the hearing. Under these conditions a second paracentesis was done, but again without the liberation of pus. The leukocyte count on the day of the second paracentesis was 17,600, and the day following, the swelling not having changed, a mastoid operation was done, exposing a small fistula near the posterior meatal wall. A large quantity of pus was found and much destruction of the mastoid process, together with a wide exposure of the dura and lateral sinus, both of which tissues appeared normal. A spinal puncture, made directly after the operation, gave negative results. Within a few days

the leukocyte count decreased, and ten days after the operation reached 10,200, the differential showing 56 per cent. neutrophils, 27 small mononuclears, 16 per cent. large mononuclears and 1 per cent. transitionals. From this point the temperature gradually subsided and the patient made an uneventful recovery, the wound closing in about seven weeks, and the hearing steadily improved during the succeeding two months until it became normal for the whispered voice. At no time before or after the operation was there any discharge from the ear by way of the external canal. The justification of the author's claim that the classification of this case is that of a primary mastoiditis is based upon the fact that, notwithstanding the evidences of pain in the left mastoid for a period of three weeks, there were no changes on objective examination of the membrana tympani and the hearing remained good; further, that two free incisions of the drum-head, made at different times, liberated no pus from the middle ear, and that there was no impairment of hearing until a time coincident with the operation and swelling over the left mastoid, at which time the hearing suddenly lessened.

The Value of the Galvanic Method of Testing the Functions of the Inner Ear and Eighth Nerve.—MACKENZIE (*Ann. Otol., Rhinol., and Laryngol.*, September, 1917). Following a review of the caloric and rotational tests of function of the labyrinth the author emphasizes the value of the galvanic test, for which certain essentials are required: A suitable electric apparatus with clean contact points; an accurate milliamperemeter; a reversing switch under the control of a capable assistant governing the polarity, the amount of current and observing the milliamperemeter; two electrodes, one about 2 inches square and flat and the other a small ball electrode, about a quarter of an inch in diameter, both electrodes being wrapped in cotton or gauze moistened with salt solution. The primary examination should be made to determine any spontaneous nystagmus, the presence or absence of which should be noted, the patient's head being tilted slightly backward to make a better observation of the eyes by the examiner, looking straight forward, with the result of looking slightly downward in consequence of the downward inclination of the head. The square electrode is held by the patient in either hand, the examiner applying the ball electrode to the tragus, pressing the tragus inward with one hand and lifting the lid of the patient's eye with the other hand in order to better observe movement. The author's conclusions from his observation of a large number of cases is that the galvanic test is more accurate than either the caloric or rotational test. Besides being more accurate the galvanic test is the least annoying to the patient, the most sensitive and the easiest to control. It can be applied as a unilateral test in all sorts of pathological conditions, which is an advantage that cannot be conceded to the caloric, and it is applicable to cases of suspected unilateral labyrinth suppuration, with obstruction in the external canal where the caloric test may fail. That it is a unilateral quantitative test, which is a distinct advantage over the rotational test, which is at best a bilateral test. That it is the only test that we possess for testing the function of the eighth nerve in cases of neuritis or cases of secondary degeneration following destruction of the inner ear, and it is the only test whereby it is

possible to make a differential diagnosis between labyrinth destruction and eighth-nerve neuritis. That it is the only test available for determining the progress of eighth-nerve neuritis, whether favorable or unfavorable, these conclusions emphasizing not the lack of value in the caloric or rotational tests, but the fact that the galvanic test is, in all respects, the best, and has a distinctive value in differential diagnosis.

An Air Raid Case.—YEARSLEY (*Jour. Laryngol., Rhinol., and Otol.*, September, 1917) records a teacher, aged twenty-seven years, who was standing by the front door of her school, superintending the passing of her class to the basement, when a bomb was dropped some yards away in the street. The door was burst open by the explosion and she was thrown down, sustaining a scalp wound. She did not lose consciousness but found that she was markedly deaf, especially in the left ear, with loud ringing tinnitus. By the next day this symptom was much improved but the impairment of hearing remained much the same. There was much difficulty in distinguishing low tones and distant sounds. There was no vertigo. On examination the right drum-head was found to be markedly indrawn and the appearance of the superior posterior quadrant suggested a perforation, the long process of the incus standing out clearly. Movement was visible, however, over the apparent perforation, suggesting the presence of a strongly indrawn flaccid posterior segment. The handle of the malleus moved freely. There was nothing noteworthy in nose, throat, or nasopharynx. The fundamental tests gave the following reactions: Weber's test showed no reference to either side. Rinné was just positive to the C 128 fork on both sides. Bone conduction to the 35 sec. fork was right 36", left 40". The hearing for low tones was right 2 C 32, left 1 C 64; that for high tones was over 15,000 double vibrations on both sides. The whispered hearing was right, 7 feet; left, 25 inches. The case appeared to be one of acute depression of the tympanic membrane from sudden increase of external pressure. The appearance of the membrane varied remarkably. The right was indrawn but it was evidently thickened. The left looked as if a very flaccid posterior segment were lying in the internal tympanic wall. It was the left ear which was toward the explosion. The functional tests indicated a middle-ear condition by increased bone conduction and loss of low tones, but not a very marked or long-standing one. Rinné reaction still positive, bone conduction only very slightly increased and no implication of the labyrinth. On using the Eustachian catheter there was no perforation sound in the left ear and the appearances noted in the tympanic membrane before inflation were less marked. The hearing for the whisper after catheterization was right, 15 feet; left, 8 feet. One month after the accident the hearing was much improved and the tinnitus was reduced to an occasional slight ringing, especially on recumbency. The hearing for the whispered voice was 15 feet for both ears and the Rinné reaction was more markedly positive on the two sides. The Eustachian catheter again failed to elicit any perforation sound. In conclusion the author remarks that it would be interesting to know the proportion of pure middle-ear cases, such as this, to labyrinthine concussion after exposure to high explosives, he having seen two similar cases in officers from the front and having heard of others.

DERMATOLOGY

UNDER THE CHARGE OF

MILTON B. HARTZELL, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

The Treatment of Keloid by Injections of Creosoted Oil.—LESIEUR (*Jour. de méd. de Paris*, May, 1918) employs injections of creosote in sterile olive oil, 10 c.c. of the former in 150 c.c. of the latter, in the treatment of keloid. The puncture is made in the sound skin close to the growth and the oil injected beneath, but not into the keloidal tissue. From 2 drops to 5 c.c. are injected at each treatment, care being taken not to overdistend the tissues; the injections are made every two days or even every day according to circumstances. There is at first a diminution, later complete disappearance of the rosy or violaceous tint of the keloid; itching and pain if present cease with the first injection; the skin becomes supple and the growth finally flattens out and disappears. These results are obtained in from fifteen days to two months; in some instances, however, it may be necessary to continue the treatment for six months. The author has employed this method of treatment in 100 cases and regards it as very satisfactory.

The Treatment of Dermatitis Venenata by Vegetable Toxins.—STRICKLER (*Jour. Cutaneous Dis.*, June, 1918) from an experimental study of dermatitis venenata concludes that the intramuscular administration of the toxins obtained from various poisonous plants influences the course of the disease although he does not advocate this procedure as a routine method of treatment and would employ it only in extremely severe cases. He believes the immunity obtained is a tissue immunity which is very transitory and must be frequently renewed. He thinks it possible to produce an endemic test by which the particular plant to which the individual is susceptible may be detected. He failed to find any complement-fixing bodies in the serum of those who had an attack of dermatitis venenata and who had been treated by injections of homologous vegetable toxins. He regards it as possible to desensitize individuals so that they may be immune from the affection. (Von Adelung, experimenting upon rabbits and guinea-pigs with poison oak, was unable to produce immunity.—M. B. H.)

Pyodermia of Parasitic Origin.—SEMON and BARBER (*British Jour. Dermatol.*, July-September, 1917) report their experience with pyogenic infection of the skin as a complication of scabies and pediculosis. They find that the disability produced by pyogenic infection is considerable, no less than 94.3 per cent. of the cases admitted to a military hospital for diseases of the skin under their care being of this nature. They find that the *Pediculus vestimentorum*, in a considerable number of cases, lays its eggs in the hair of the pubis, the perineum and sometimes of the axillæ and other hairy regions, therefore disinfection of the clothing alone is not sufficient to get rid of the parasites, but the

host himself should be disinfected. They regard it as extremely probable that the pyogenic lesions in pediculosis begin around the bite of the pediculus. The severity of the lesions, especially in scabies, is very much increased by the presence of seborrheic diathesis, the itch mite under such circumstances being a most potent agent in producing an acute seborrheic dermatitis. Pyoderma accompanying scabies or pediculosis usually recovers rapidly if the cause is recognized and appropriate treatment adopted.

Ulcerating Granuloma of the Pudenda.—PARDO (*Jour. Cutan. Dis.*, April, 1918) reports 2 cases of this malady, the first to be reported in Cuba. The first patient was a young mulatto woman, aged twenty-four years. An extensive ulceropapillomatous area, with sharply defined and elevated borders, occupied the groins, the vulva, the perineum and the anal region. The disease had begun five years before as a small sore on the right labium majus, which had slowly extended in all directions. A month's treatment with salvarsan (three injections) and potassium permanganate solution, 1 to 1000 locally, having failed to produce any improvement, intravenous injections of tartrate of antimony and potassium were resorted to, 5 c.c. of a 1 per cent. solution being given every other day. Improvement was observed after the fourth injection and continued until, at the end of five months, cicatrization was almost complete. As the patient then passed from observation the final result was unknown. Similar treatment was begun in the second case, a white man, aged twenty-five years; but as he did not return after the first injection there was no further opportunity to follow up the case. Although the first and only cases recorded thus far in Cuba, the author believes the malady is not uncommon in the island, since he has been told of the existence of similar cases by country practitioners, especially in the eastern part.

A Common Origin for Shingles and Chicken-pox.—LE FEUVRE (*British Jour. Dermatol.*, October-December, 1917) believes there is a close etiological relationship between herpes zoster and chicken-pox. He has collected about 50 cases, 7 of which were under his own observation, in which these diseases occurred so closely associated as to suggest the probability that they had a common origin. In the author's 7 cases an attack of zoster was followed in from twelve to twenty days by chicken-pox in some other member of the family, in all cases a child. Of the whole number of cases collected 41 showed this sequence, while in a much smaller number (5 cases) zoster followed the chicken-pox; in 4 cases the two diseases were concurrent. The author believes shingles to be an infectious disease, which, under certain unknown conditions, may serve as the starting-point for an epidemic of chicken-pox, and should therefore be placed in the list of notifiable diseases.

Treatment of Psoriasis by Intramuscular Injections of Pure Sulphur in Solution.—BORG (*La Presse méd.*, June 7, 1917) has obtained encouraging results in the treatment of psoriasis from injections of sulphur in oily solution. For these injections he has employed the following formulæ: Sulphur precip. pur., 20 gm.; ol. sesami (or

paraffin liquid), 100 c.c.; or sulphur. precip. pur., 20 cgm.; ol. eucalyptol., 20 c.c.; ol. sesami, 80 c.c. Of these solutions he gave 5 c.c. at a dose, the equivalent of 1 cgm., making the injections deeply into the gluteal muscles. One case was cured by one injection, one by four injections and a third improved after eight injections. As only 5 cases have as yet been treated, definite conclusions concerning the value of the treatment are not yet possible.

Eczema Due to Deficient Thyroid Secretion.—EDELMAN (*New York Med. Jour.*, March 9, 1918) reports the following unusually interesting case: A boy, previously apparently in good health developed, when four years old, a more or less general eczematous eruption in places dry and scaly, in others moist or weeping, accompanied by severe itching, which was worse at night. This eruption continued unabated notwithstanding much treatment, both local and dietetic, at the hands of pediatricists and dermatologists, until he was three and a half years old. When he first came under the author's observation he was fairly well nourished, but presented a cretinoid facies, had a pasty color and a general adenopathy. There was no body hair, the brows were scanty, but the hair of the scalp was coarse and abundant. The patient was placed upon thyroid extract three times a day, without any local or dietetic treatment, and improvement began at once, so that within five days "the eczema of the face and neck had almost disappeared." This improvement continued for another week when owing to rapid loss of weight, the thyroid was stopped and local and dietetic treatment instituted. When seen again the eruption was very much worse and the thyroid was again given with markedly beneficial results as before. Improvement continued, and when last seen the boy was normal in every respect. The author believes hypothyroidism was wholly responsible for the eczema, an opinion supported by the remarkably prompt improvement following the administration of thyroid extract and the equally prompt relapse following its suspension. He believes that thyroid should be given in eczema only when definitely indicated by other symptoms, and that it should be given in fairly large doses at first, to be followed later by smaller ones to prevent relapse.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

Quantitative Relationship between Antigen Dose and Antibody Production.—The question of whether the amount of antigen introduced into an animal has any bearing upon the extent of the immune reaction has been repeatedly discussed in relation to specific types of antibodies.

TSEN (*Jour. Med. Res.*, 1918, xxxvii, 381) has brought forward evidence that no such quantitative relationship between the antigen dose and antibody exists. His conclusions are drawn from a series of experiments in which precipitins and agglutinins were quantitatively estimated. The precipitins were obtained by intravenous injection of different doses of sheep serum into rabbits, while the agglutinins were obtained in the human after the administration of antityphoid vaccine. He points out that individuals differ greatly in their response to the injection of foreign proteins, but the injection of large quantities is no guarantee of the production of large amounts of antibody. To a certain extent the potency of a serum in antibody rests in the manner of the giving as well as in the individual response of the animal tissues.

Chronic Tonsil Infections.—MOORE (*Jour. Lab. and Clin. Med.*, 1918, iii, 283) offers a discussion on chronic infections of tonsils based upon the work of various investigators. He describes the anatomical structure of the tonsil, and he points out that because of its position and structure the tonsil is more prone to infection than almost any other organ in the body. Because of its position it comes in contact with the various species of bacteria in the mouth cavity. More important than this, however, is the deposition of these bacteria with food and other débris in the lumina of the crypts. Chief among the bacteria causing either acute or chronic tonsillitis is the streptococcus. Davis isolated hemolytic streptococci in the majority of 133 cases of tonsillitis which he studied. The patients had been suffering from chronic arthritis, endocarditis and nephritis, and although this streptococcus produced arthritis in rabbits, there is no proof that it is the causative factor. In almost all tonsils, pathological or not, hemolytic streptococci producing arthritis in rabbits can be isolated. The author here refers to Rosenow's theory that bacteria isolated from the apparent focus of infection will produce similar lesions in animals. Tuberculosis and syphilis are of considerable interest as chronic infections. Out of the author's series of 250 pairs of tonsils, tuberculosis was present in 2.5 per cent. Primary tuberculosis of the tonsil varies from 1 to 5 per cent., and the tubercle bacillus is rarely found in tonsillar crypts. Syphilis of the tonsil may be primary, secondary or tertiary, and varies from 6 to 55 per cent., women being most commonly affected. Actinomycosis of the tonsil has been occasionally described. Davis thinks no well-authenticated case of primary actinomycosis of tonsil has been reported. Diphtheroids are not uncommon as infective agents. Occasionally the pneumococcus is isolated as well as the staphylococcus, *B. diphtheria*, *B. influenza* and *B. mucosus capsulatus*. The author emphasizes the importance of the tonsil as a portal of entry for numerous infectious organisms and that its removal may aid materially in controlling such diseases.

The Production of Antipneumococcus Serum.—COLE and MOORE (*Jour. Exper. Med.*, 1917, xxvi, 537). All kinds of animals, even the most susceptible, may be rendered actively immune to pneumococcus infection by bacterial inoculations. In the production of immune serum for therapeutic purposes strict attention must be paid to the immunological specificity of the bacteria used for immunization. At present the only serum of which the therapeutic value has been proved is that

effective against Type I pneumococcus infection. Active immunity to the different types also seems very specific. The serum to be used should have agglutinating power for Type I pneumococcus and should have the power of protecting mice against large amounts of virulent culture. For therapeutic purposes one should use the horse, which is sound and healthy and without old joint injuries. The intravenous method of injecting the culture is the most valuable one. Experiments have shown that for producing the primary immunity most rapidly several series of small doses of dead cultures should be given, the injections being made daily for six to seven days followed by a week in which no injections are made. To produce the highest type of immunity living organisms are required. The virulence of the particular strain of pneumococci used for inoculation purposes is important, and this virulence should be preserved by repeated animal inoculations and only fresh cultures are to be used for the immediate injection. The living organisms should be given in moderate doses daily for three days, with an interval of a week between each series of injections. By following the methods here described, horses may be made to produce rapidly a high grade of specific serum. The observations made in this work indicate the importance of employing small doses of culture frequently repeated in this form of immunization.

Anticomplementary Power of Human Serum and the Wassermann Reaction.—In 1914 Nicolas and Gate pointed out that the anticomplementary power of human serum frequently prevents hemolysis of red blood cells in the course of the Wassermann reaction. It is necessary therefore to neutralize entirely and exactly the anticomplementary action if one wishes to obtain a pure Wassermann reaction. HOLLANDE (*Jour. de Physiol. et de pathol. générale*, 1917, xvii, 684) decided to determine methodically the anticomplementary power of each serum before doing a Wassermann. The author determined the quantity of titrated complement which should be added to a constant volume of the inactivated serum in order that its antihemolytic action be neutralized. The quantity of complement which is necessary and sufficient for total hemolysis constitutes what the author calls the "constant complement," representing the exact quantity of complement which is necessary to neutralize the anticomplementary power of the serum of disease and bring about hemolysis. In thus always determining the anticomplementary power of the serum before proceeding with the Wassermann reaction the author found that 8 per cent. of the sera have a constant complement. The anticomplementary power of the serum seemed to correspond to the increase of the albuminous substances: the presence in the serum of natural hemolysins against the red blood cells of sheep tends, on the contrary, to diminish this power.

Preservation of Antisheep Hemolytic Amboceptor in Glycerol.—The hemolytic system is very widely used as an indicator in determining whether a specific type of amboceptor or antigen is present in a given material. In practice the use of the indicator has mainly fallen to the technic of the Wassermann reaction and the tests on the binding of complement in the presence of the immune bodies in the serum of suspected cases of gonorrhoea, typhoid fever and a few other infections.

Inasmuch as the hemolytic system serves as a indicator it is essential that its component parts be as stable and constant as possible. The chemist has his various color reactions which serve as indicators for the detection of certain definite substances. In the case of the hemolytic system the indicator is not a single substance but a group of them. Each of which has labile quantities. It is because of the danger of deterioration and change in the components of this indicator that the greatest care is necessary before using them in any given test. Investigators have found that when amboceptor is stored in the fluid state, it is liable to undergo deterioration with varying rapidity. There is also constant danger that the serum will become infected during storage and use. To prevent infection various mild antiseptics as thymol, camphor and chloroform have been used, but again discarded by most workers because of changes occurring in the serum in their presence. CLOCK and BEARD (*Jour. Infect. Dis.*, 1917, xxi, 404) have experimented with glycerol as a preservative for the hemolytic amboceptor and find that it offers many advantages. When mixed with an equal amount of fresh amboceptor heated to 55° C. the serum was found to retain its original potency for three years. No anticomplementary properties developed during this period. The presence of the glycerol did not influence the complement-fixation reaction. The presence of the glycerol presented bacterial growth similar to its action when used in vaccine lymph.

Food Accessory Factors (Vitamins) in Bacterial Culture with Especial Reference to Hemophilic Bacilli.—It is now generally conceded that food accessory factors (vitamins) are as essential for proper development and maintenance of health as proteins, carbohydrates, fats and salts. They also play an important part in the nutrition of the lower forms of animal life, of the higher plants and of bacteria. Various investigators have carried on experiments with yeast, peat and the hemophilic bacteria. Pfeiffer in 1892 made the discovery that not only blood was necessary for the continued growth of the influenza bacillus but also that hemoglobin was the essential constituent in the blood upon which growth depended. In further investigation, DAVIS (*Jour. Infect. Dis.*, 1917, xxi, 392) found that hemoglobin alone will not support growth but that a second factor which resides in many bacteria, fresh animals and plant tissues is necessary. This second substance is being studied further to determine its peculiar properties which at present are not clearly defined. The availability of iron in the hemoglobin may be the determining factor in the growth of hemophilic bacteria and the second factor or substance may act by rendering this element more available. The suggestion may be made, in conclusion, that the activity of these substances in animals and higher plants may concern or somehow control the metabolism of certain elements like iron, phosphorus, calcium or iodine, as well as possible of protein.

Cases of Typical and Atypical Lymphosarcoma.—MACKENZIE (*Jour. Cancer Res.*, 1918, iii, 93) reports 4 cases of lymphosarcoma taken from the autopsy records of the past five years. Two may be classified as typical, since they conform with the characteristics of lymphosarcoma laid down by MacCallum, Sternberg, Paltauf and

Kundrat. Briefly these are tumor formation starting in a group of lymph nodes and spreading thence to neighboring nodes or follicles, with no general lymphoid involvement as in leukemia or pseudo-leukemia. True metastases by way of the blood stream are rare and usually isolated. The commonest sites of origin are the lymph nodes of the neck, mediastinum, mesenteric and retroperitoneal regions, less frequently the inguinal and axillary nodes. The affected groups form nodular, uneven masses, well limited in the beginning but later diffusely permeating the surroundings. The spleen and bone marrow are rarely attacked. Histologically the tumor is characterized by an irregular reticular framework with lymphoid cells in the meshes. The cells resemble lymphocytes but are larger and have a more lightly staining nucleus and a scanty, often almost invisible non-granular cytoplasm. There is no definite alteration of the blood picture. The other two cases not falling in this category, resembling each other in pathological anatomy and histological picture, are atypical lymphosarcomata. The main points which distinguish them from true lymphosarcomata are the early involvement of the lymph nodes throughout the body in a manner not suggesting regional extension, the distinct nodular metastases in liver and spleen, the inability to grow out into the surrounding tissue and the different cell components. The neoplasm is not leukosarcoma in which the splenic enlargement is due to a diffuse infiltration of the whole spleen by the abnormal cells and not to the presence of distinct nodules. It is hardly necessary to point out that the histological picture of Hodgkin's disease alone is sufficiently characteristic to make it unnecessary to indicate other points of differentiation.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,
WASHINGTON, D. C.

Hog Cholera and Paratyphoid Fever. Studies on the Paratyphoid-enteritidis Group.—KOHNS and VALENTINE (*Jour. Med. Res.*, March, 1918, pp. 89-125) state that the tendency to variations, as well as the differences in avidity for carbohydrates, shown by otherwise similar types, has led to contradictory opinions as to the classifying significance of the cultural reactions of members of the paratyphoid-enteritidis group. By correlating the fermentative results, especially in relation to quantitative reductional differences, well-defined groups result, as shown in the tables presented. This grouping correlates

host origin and agglutinative differences. *Bacillus cholerae suis* and *Bacillus paratyphosus* "B" in this way are separable one from the other, and the *Bacillus cholerae suis* is therefore a distinct type, and most of the strains studied have been similar and constitute a definite subgroup. This indicates that *Bacillus paratyphosus* "B" is essentially a human pathogen and that paratyphoid fever due to this type is normally caused by the transfer of the bacillus from man to man, and that infected swine are not a source of contagion for this disease, either directly or indirectly, through the consumption of infected food.

Observations on Meningococcus Carriers and on the Bacteriology of Epidemic Meningitis. — During the summer and fall of 1917 MATHERS and HERROLD (*Jour. Infec. Dis.*, June, 1918, No. 6, xxii, 523) made an extensive bacteriological study of epidemic meningitis in one of the large military camps. The meningococcus carriers in the infected organizations were identified and isolated. For the cultures plain blood-agar was found to be satisfactory and the material for culture was obtained from the nasopharynx by means of a simple uncovered wire swab. It was found that 3 to 6 per cent. of the men examined were meningococcus carriers. The majority of these carriers, however, were of the temporary type; only 1.2 per cent. of the total number of suspects examined proved to be chronic carriers. Chronic meningococcus carriers, as distinguished from the temporary type, often harbor great numbers of meningococci in the secretions of the nose and throat. The number of carriers was found to be high among those coming in contact with meningitis cases. In a study of the biological reactions of 150 strains of meningococci from different sources two large biological groups were differentiated by means of macroscopic agglutination tests using monovalent serums. The agglutination reactions were in most instances definite and specific, but a number of atypical and inagglutinable strains were met with in each group. The atypical strains, however, did not differ enough from the other members of the group to warrant different classification as determined by agglutination. The classification of the inagglutinable strains was accomplished by means of agglutination with monovalent serums prepared from these strains; these serums yielded specific reactions with organisms of one or the other main type. The biological type of meningococcus predominant in the camp epidemic was identical with the type prevailing among the chronic carriers, but different from the type of meningococcus, causing the majority of the sporadic cases of cerebrospinal fever in Chicago. Also the type of meningococcus found in the cases and in the corresponding immediate contacts was in every instance the same. These facts suggest there is a close relationship between cases of epidemic meningitis and meningococcus carriers.

The Value of the Wassermann Reaction. — LARKIN, LEVY and FORDYCE (*Jour. Am. Med. Assn.*, June 1, 1918, No. 22, lxx, 1589) state that the term "Wassermann reaction" includes several methods of serological procedure. An accurate interpretation of each method is essential in arriving at a proper diagnosis. A positive reaction is the most constant symptom of syphilis. The value of the reaction in diagnosing undoubted syphilis is shown by the following facts: (1)

The reaction is positive in practically 100 per cent. of the cases of florid syphilis. (2) In active tertiary syphilis of the skin and bones the reaction is positive in about 94 per cent. of the cases. (3) In syphilis of the central nervous system cognizance must be taken of the reaction in both blood and spinal fluid; the blood is positive in 80 per cent. of the cases. (4) In a pathological study the Wassermann reaction (alcoholic antigen, warm fixation) was positive in 94 per cent. of cases of syphilitic aortitis. As a means of corroborating syphilitic infection the Wassermann test is at least 90 per cent. dependable, as shown in a series of positive reactions in which 90 per cent. could be accounted for by syphilitic changes in the aorta alone. The value of a negative reaction has been studied and its reliability confirmed by the negative reactions obtained in non-syphilitic affections of the skin. In a series of necropsies in which it was demonstrated pathologically that the aorta was free from syphilitic disease, negative reactions were obtained in 91 per cent.

Presence of Tubercle Bacilli in the Feces of Cattle in Dairy Herds.

—WILLIAMS, SCOTT, ROBERTS and HOY (*Veterinary News*, April 28, 1917, No. 695, xlv) state that this research is a preliminary to testing the viability of the tubercle bacillus when excreted on pasture land in the feces of cows. Incidentally it revealed a means whereby milk may become infected with tubercle bacilli from dung. To test the excretion of bacilli, guinea-pigs were inoculated with an emulsion of the feces. In all samples of the feces of 179 cows were examined, but for various reasons some of these were excluded from the final results. After such exclusions it was found that virulent tubercle bacilli were present in the feces in 3 cows out of 158. It is possible that one of these infecting cows should also be excluded, as she had been operated upon for tuberculous glands in the neck twelve months before the sample of feces was taken and was again obviously unwell. If, then, this animal be also excluded there remain 2 apparently sound cows whose feces infected guinea-pigs with tuberculosis from among 157 which were examined. By other methods it is possible that other cows might have been found to excrete tubercle bacilli in their feces. Only one sample was taken from any animal, and the sample represented only a very small fraction of the total daily excrement. Moreover, only a fraction of the sample taken could be inoculated into guinea-pigs.

Tuberculous Mastitis in the Cow, Its Pathogenesis and Morbid Anatomy and Histology.

—McFADYEAN (*Jour. Comp. Path. and Therap.*, March, 1917, Part I, xxx) discusses the three views representing the route of infection of the mammary gland, namely: (1) by way of the milk canals; (2) by the blood stream from a preëxisting focus; (3) by way of the lymphatics from some tuberculous lesion in the abdomen. Against the theory of embolic infection are certain features of mammary tuberculosis: (1) The disease, as a rule, begins in one quarter of the udder and not in all four quarters. (2) In the great majority of cases it is a hindquarter which is first attacked. (3) The disease generally appears to have begun at the upper part of a quarter. (4) As a rule the lesions do not appear to develop from separate discrete centers in the quarter first attacked. (5) In certain cases, which are by no means rare, the supramammary lymph glands are found to be visibly tuberculous

while the entire udder tissue appears to be normal. The lymphatic theory, on the contrary, affords a perfectly satisfactory explanation of the whole of these facts. Infection through the teat canal is possible but rare. Attention is called to the common error in supposing that tuberculous mastitis is a nodular disease and that consequently palpation of a suspected udder should be directed to the detection of firm nodules. The disease is diffuse and increased solidity and firmness, without the formation of actual tubercles, are the more constant characters of the lesions.

The Four Essential Factors in the Production of Milk of Low Bacterial Content.—AYERS, COOK and CLEMMER (*Bull. No. 642, U. S. Department of Agriculture*) point out that the production of milk of a high sanitary quality involves a knowledge of the influence of numerous factors. To deal intelligently, therefore, with the influence of these factors, they must be grouped so as to bring together those which are of importance in connection with some definite phase of production. With this thought in mind the following group of factors were selected as a means of clarifying the subject. (1) Factors concerned in the production of milk which is practically free from visible dirt and which has a low bacterial content. (2) Factors most directly concerned in the prevention of infection of milk with pathogenic organisms. (3) Factors of importance in connection with the health of cattle. (4) Factors concerned in providing and maintaining conditions suitable for the production of a food product, even though they may not directly effect the quality of the product. The paper considers only the factors in group one. The experiments were conducted in a small barn with four cows. The general plan of the work, which covered about one and a half years, was as follows: At first the barn and cows were as dirty as possible, then one factor of improvement at a time was introduced, in order to obtain a milk of low bacterial content. When the essential factors were determined their value was checked by repeating the experiments. Extensive information is given in the paper on the contamination of milk by unsterilized utensils and manure and also the growth of bacteria in milk held at different temperatures. The experiments showed that the unsterilized utensils were a much greater source of contamination than manure and dirt. It is pointed out, however, that manure and dirt should be kept out of milk not only from a stand-point of common decency but because it assists in producing milk of low bacterial content and reduces the possibility of infection by disease-producing organisms, such as that of bovine tuberculosis. The results of the experiments indicate that it is possible for the average dairyman on the average farm, without expensive barns and equipment, to produce milk (practically free from visible dirt) which when fresh has a low bacterial count. By the use of three simple factors, which named in order of importance are sterilized utensils, clean cows with clean udders and teats, and the small-top pail, it should be possible on the average farm to produce milk which corresponds closely to milk as it leaves the udder of the cow. With these three factors it was possible during a period of two months to produce milk in an ordinary barn, 65 samples of which, when fresh showed an average count of 2154 bacteria per cubic centimeter. The value of these three factors

was demonstrated under practical conditions on six farms. A fourth factor of holding milk as near 10° C. (50° F.) is also absolutely necessary and increases in importance with the age of the milk. In connection with the production of milk of low bacterial content it seems evident from the results that undue emphasis has been given to factors and methods of minor importance, while those which directly affect the bacterial content have not been sufficiently emphasized.

Physiological Stimulation of the Choroid Plexus and Experimental Poliomyelitis.—FLEXNER, AMOSS and EBERSON (*Jour. Exp. Med.*, June 1, 1918, No. 6, xxvii, 679) record experiments which serve, in the first place, to confirm those of Dixon and Halliburton on the stimulating effect of intravenous injections of extracts of choroid plexus in the secretion of cerebrospinal fluid and extend their observations to monkeys. They bring out also the variable effects of the virus of poliomyelitis, variations affected by the quality of the virus and also by the individual powers of resistance to infection possessed by individual monkeys. These factors of variation must be taken into account in performing and interpreting experiments on infection and particularly those on immunity and specific therapy in relation to poliomyelitis. In general it may be said that experimental infection by way of the blood is not easy to produce in monkeys unless some contributing factor, such as the existence of a coincident aseptic meningitis, operates at the same time. And yet two of their experiments show that when the strength of the virus is great the injection of relatively considerable quantities suffices to induce infection and paralysis, but not in all instances. The chief outcome of the experiments has been to determine the fact that when the intravenous inoculation of the virus does not in itself suffice to induce infection and paralysis the intravenous injection of extracts of the choroid plexus, which in themselves excite the secretory functions which preside over the formation of the cerebrospinal fluid, is powerless to modify this result. This fact would seem to be of interest and importance, since it has already been shown that very slight structural changes in the meningeal-choroidal complex suffice to make possible or certain infection under these circumstances. Apparently mere augmentation, from time to time, of the secretory functions of the choroid plexus, through intravenous injection of an extract of the choroid plexus and while the virus is still circulating, is insufficient to ensure passage of the virus from the blood into the nervous tissues, upon which infection depends. Neither does the augmentation exercise a restraining influence on the development of infection otherwise capable of taking place.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

OCTOBER, 1918

ORIGINAL ARTICLES

**A HUGE HEMANGIOMA OF THE LIVER ASSOCIATED WITH
HEMANGIOMATA OF THE SKULL AND BILATERAL
CYSTIC ADRENALS.**

BY RALPH H. MAJOR, M.D.,

AND

DONALD R. BLACK, M.D.,

ROSEDALE, KANSAS.

(From the Department of Pathology, University of Kansas School of Medicine,
Rosedale, Kansas.)

HEMANGIOMATA of the liver are by no means rare tumors and are probably the most common and best known of all new growths in this organ. In the majority of cases these tumors are small, cause no clinical symptoms and are discovered first at autopsy. The following case, however, seems worthy of record because of the immense size of the hemangioma, its clinical course and its association with similar tumors of the skull and an unusual condition in both adrenals.

CASE HISTORY.—The patient, A. R., a man, aged thirty-four years, entered St. Margaret's Hospital, service of Dr. P. T. Bohan, on February 15, 1915, complaining of swelling of the abdomen. He had been apparently in perfect health until the age of eighteen, when he noticed that his abdomen was somewhat increased in size. During the past fourteen years it has continued to enlarge until upon admission it had reached the size shown in Fig. 1. He also states the interesting fact that a nephew, aged seven years, has a similar enlargement of the abdomen.

Physical examination showed a large irregular mass in the abdomen, with marked ascites and edema of the ankles. The blood examination showed red blood cells, 3,200,000; white blood cells, 4500; hemoglobin, 52 per cent. (Sahli); Wassermann, negative. The urine contained a trace of albumin and a few granular and epithelial casts.



FIG. 1.—Patient on admission.

The patient was under observation for over two years. During this time the blood and urinary findings remained fairly constant. The ascites increased, which made a possible enlargement of the mass difficult to determine. No jaundice developed. The patient died on September 11, 1917, and the autopsy was performed five hours after death. Two hours before the autopsy the body was injected with embalming fluid through the femoral veins.

Autopsy showed the most interesting findings to be in the liver, the skull and the adrenals. Each of these will be subsequently

discussed in order and the results of the macroscopic and microscopic examinations considered. In addition to these findings the body showed an ascites, atelectasis of the lower lobes of both lungs and granular kidneys. The heart, spleen, stomach, pancreas, intestines and bladder showed nothing specially abnormal.

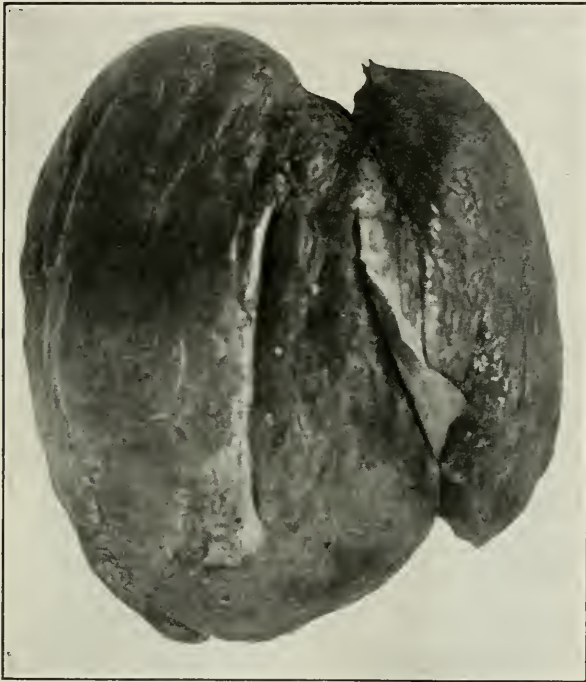


FIG. 2.—Liver of patient.

THE LIVER. The liver (Fig. 2) was greatly enlarged and extended 40 cm. below the xiphoid process of the sternum in the midline. It measured 35 x 44 x 11 cm. and weighed 18,160 grams. The organ was of a dark reddish-purple color, the surface was uneven, somewhat nodular, and the capsule was covered in places with a thick deposit of fibrin. On cut section most of the liver tissue was replaced by a spongy network, in the interstices of which was clotted blood. Here and there were numerous small areas of whitish tissue scattered about which apparently were the remnants of the liver tissue. These areas of liver tissue were largest in the left lobe, where one area measuring 9 x 10 cm. was noted. Throughout the rest of the liver these areas were much smaller, varying from 1 mm. to 2 cm. in diameter, and the hemangiomatous involvement was so extensive that it was often necessary to study the cut

surface very closely in order to make out the remnants of liver tissue. The diagnosis of an extensive hemangiomatous process in the liver was apparent from the naked-eye examination.

The size and extent of the hemangioma make the specimen one of considerable interest. In the majority of cases these tumors are not of sufficient size to produce any general enlargement of the liver or cause any symptoms. Virchow¹ stated in his classic lectures on hemangioma that "as large as the tumor becomes there results, however, no increase in volume of the liver, since the destruction of liver tissue keeps pace with the growing angioma." The largest hemangioma he described measured 3.5 x 4 cm. Schmieden² studied 32 cases of hemangioma of the liver, all of which were accidental findings at autopsy and produced no symptoms during life. There are, however, certain cases reported in which the tumor reached a considerable size. Payne³ reported a case in which the liver showed numerous hemangiomata and weighed 2700 grams (6 pounds).

Langhans⁴ described a case of hemangioma of the liver associated with a similar tumor of the spleen. The liver in his case measured 30 x 30 x 18 cm. and was roughly three or four times the normal size. Von Eiselsberg⁵ removed a hemangioma of the liver which weighed 470 grams. Birch-Hirschfeld⁶ saw a patient in whom the liver hemangioma was so large that the abdomen resembled that of a pregnant woman.

Pfannenstiel⁷ operated upon a patient and removed a liver hemangioma weighing approximately 5290 grams (12 Pfund). Langer⁸ extirpated a similar tumor which measured 21 x 21 x 11 cm. and weighed 5000 grams. Phillipini⁹ described a hemangioma of the liver the size of a human head. In Mantle's¹⁰ case the tumor measured 30 x 16 x 4 cm. (12 x 6½ x 1½ inches) and involved the greater part of the right lobe of the liver. Von Genersich¹¹ saw a tumor as large as a child's head. Chiari¹² described one as large

¹ Die Krankhaften Geschwülste, Berlin, 1863, Bd. iii, p. 393.

² Ueber den Bau und die Genese der Lebercavernome, Arch. f. path. Anat., 1900, cxi, 373.

³ Vascular Tumors of the Liver, Suprarenal Capsules and Other Organs, Tr. Path. Soc., London, 1869, xx, 203.

⁴ Casuistische Beiträge zur Lehre von den Gefässgeschwülsten, Arch. f. path. Anat., 1879, lxxv, 273.

⁵ Quoted by Langer.⁸

⁶ Lehrbuch der pathologischen Anatomie, 1895, Band ii, Heft 2, p. 739.

⁷ Erfolgreiche Extirpation eines grossen cavernösen Leberangioms, Allg. med. Centr. Ztg., 1898, lxvi, 1.

⁸ Erfolgreiche Extirpation eines grossen Hemangioms der Leber, Arch. f. klin. Chir., 1901, lxiv, 630.

⁹ Resection of the Liver, British Med. Jour., 1901, II Epitome of Current Medical Literature, p. 22.

¹⁰ An Unusually Large Angioma of the Liver, British Med. Jour., 1903, i, 365.

¹¹ Operierter Fall eines kindskopfgrossen Angioma Cavernosum hepatis, Med. Klin., 1908, iv, ii, 1722.

¹² Tumor cavernosus, München. med. Wchnschr., 1909, lvi, 1615.

as a man's head. Roggenbau¹³ studied a huge hemangioma of the liver measuring 22 x 9 x 33 cm. This case is apparently the same as that reported by Chiari. M'Weeney¹⁴ reported a case in which the liver was much enlarged, weighing 5100 grams (180 ounces) and the entire left lobe was transformed into an angiomatous mass measuring 25 x 25 x 10 cm. MacCallum¹⁵ mentioned a huge hemangioma of the liver which hung by a stalk from the right lobe and measured 24 cm. in diameter.

These are the largest hemangiomata of the liver that we have found in the literature. In none of these cases was the tumor as large as in our case. Our specimen had produced such an enlargement of the liver that it weighed ten times the normal weight and constituted nearly one-half (4.9) of the patient's entire weight.

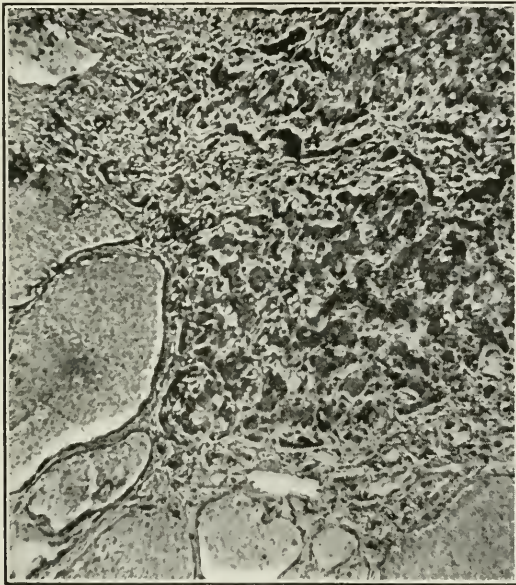


FIG. 3.—Microscopic picture of a liver tumor. Zeiss obj. AA, oc. 4.

The microscopic examination of the liver tumor presented interesting pictures which varied somewhat in different parts of the tumor. A common picture (Fig. 3) was that of large dilated spaces filled with blood lying against collections of liver cells, which were often compressed and showed definite evidences of fatty degeneration. In some parts of the tumor small lobules of the liver were surrounded by a dense overgrowth of connective tissue, which

¹³ Zur Kenntnis der cavernösen Angiome der Leber, Beitr. z. path. Anat., 1910, xlix, 313.

¹⁴ Enormous Angioma of the Liver, Jour. Path. and Bacteriol., 1911-12, xvi, 401.

¹⁵ A Text-book of Pathology, Philadelphia, 1917, p. 901.

produced a picture suggesting strongly the earlier stages of a cirrhosis of the liver. The connective tissue in such pictures showed marked evidences of proliferation. There were very numerous fibroblasts present and in addition many sprouting and newly formed capillaries of various sizes. These young capillaries varied in appearance from solid tubes of cells to capillaries of increased lumen, some of which showed a degree of distention similar to the cavernous bloodvessels so characteristic of hemangiomata.

In the majority of the section examined the microscopic picture which predominated was that of the large cavernous spaces, with, as a rule, little liver tissue present. The walls of these spaces were formed by endothelium supported by a framework of connective tissue and smooth muscle. Here also there were definite evidences of growth, fibroblasts were numerous and there were many new sprouts sent out from the walls.

Ever since Virchow's studies upon hemangiomata there has been an active discussion as to the genesis and mode of growth of these tumors in the liver. It is beyond the limits of this paper to discuss these various views in any great detail. A brief summary, however, may prove of some interest.

Virchow¹⁶ stated that "the process begins with an increase of the connective tissue of the liver, which is very soon followed by a disappearance of the secretory parts of the organ. In the young connective tissue the vessels dilate and their walls become thickened and fuse with the surrounding connective tissue." This view, that the development of these tumors is caused primarily by a new growth of connective tissue, was also shared by Rindfleisch¹⁷ and by Burekhard,¹⁸ who also mention as important the accompanying "cavernous metamorphosis of the bloodvessels."

Multiple hemorrhages in the liver have been regarded by some as the starting-point in the development of hemangiomata of the liver, while Scheffen¹⁹ considered a passive venous congestion of the liver could produce in time a dilatation of the bloodvessels into cavernous spaces. Beneke²⁰ described a liver in which a congestion of bile had produced a dilatation of the bile capillaries and compression of the liver cells. He considered the picture to be that of a beginning liver cavernoma.

Ribbert²¹ considers hemangiomata of the liver as true new growths which arise from misplacement of tissue and vascular areas

¹⁶ Loc. cit.

¹⁷ Lehrbuch der pathologischen Gewebelehre, 1886, VI Aufl., p. 504.

¹⁸ Beitr. zur pathologischen Anatomie des cavernösen Angioms der Leber, Inaugural Dissertation, Würzburg, 1894.

¹⁹ Beitr. zur Histogenese der Lebereavnome, Inaugural Dissertation, Bonn, 1897 (quoted by Schmieden²).

²⁰ Zur Genese der Leberangiome, Arch. f. path. Anat., 1890, cxix, 76.

²¹ Ueber Bau Wachstum und Genese der Angiome nebst Bemerkungen über Cystenbildung, Arch. f. path. Anat., 1898, cli, 381.

in the liver as the result of a developmental disturbance. Schmieden²² states that cavernoma of the liver are caused by a local transposition of liver tissue which later develops into a tumor-like growth. A growth, however, like that of a genuine bloodvessel tumor does not occur according to his views.

The views of Ribbert and Schmieden have found the greatest number of adherents. Borst²³ states that the cause of most liver hemangiomas is to be found in an embryonal misplacement of liver tissue and that a new growth of bloodvessels cannot usually be demonstrated. For this type of tumor he prefers the name "hamartoma," introduced by Albrecht. However, he adds that "it must be admitted that genuine cavernous 'angioblastomata' of the liver do occur, but they are rarely found. In these cases one finds evidences of growth in the form of endothelial sprouts and tubes." Roggenbau²⁴ accepts the views of Borst, but has, however, reported careful studies of 2 cases of cavernous angioma of the liver which were examples of genuine new growths.

In our case the evidence is strong that we are dealing with an example of a genuine cavernous angioblastoma in the sense of Borst. The microscopic picture of forming and newly formed capillaries in the young connective tissue between liver lobules indicates active growth, as do the endothelial sprouts which are growing out from the walls of the larger blood sinuses. The gross picture of the liver with such a large amount of the liver parenchyma replaced by cavernous blood spaces is strongly suggestive of an invasive growth, and the suggestion that this process of invasion has been gradual finds support in the clinical picture of a slowly enlarging liver.

In several places the remnants of liver tissue were stained deeply with bile, and these areas were examined carefully to see if pictures could be seen which would substantiate the view of Beneke²⁵ that a congestion of bile plays a role in the formation of hemangiomas. In these bile-stained areas there were many compressed bile capillaries and ducts and others very widely dilated. The dilated bile ducts were often as large as some of the smaller cavernous spaces, but they contained no blood, and no evidence was found that they formed such blood spaces.

THE SKULL. The next autopsy findings of interest were the changes in the skull. The patient had two prominences: one over the left eye, measuring 3 x 4 cm. in diameter, and another over the right temple, measuring 2 x 3 cm. in diameter. These two prominences were apparently firmly attached to the skull and were as hard as bone. On stripping down the scalp over the right

²² Loc. cit.

²³ *Echte Geschwülste (Blastome) in Aschoff's pathologische Anatomie, 1911, II Aufl., p. 671.*

²⁴ Loc. cit.

²⁵ Loc. cit.

temple a piece of the temporal bone, including the elevated area, was removed for study.

Examination of the fragment of temporal bone showed that the swelling was produced by a thickening of the bone at that place. This thickening, however, was largely due to an unusually spongy condition of the bone, and with the naked eye large spaces filled with blood could be seen. The microscopic picture showed numerous large blood spaces filled with blood. In some places these spaces lay directly upon the bone, in other places they gave the appearance of dilated bloodvessels coursing in the bone-marrow. Another picture also frequently noted was the presence of large dilated blood-



FIG. 4.—Microscopic picture of a tumor of the skull. Zeiss obj. A2, oc. 4.

vessels surrounded by fibrous tissue, which in turn was lying upon the bone. This picture seems analogous to that in the liver, where the cavernous blood spaces show a markedly developed connective-tissue framework lying against the liver cells (Fig. 4).

The association of hemangiomata of the liver, with similar tumors in other organs, has often been noted. Payne²⁶ described a hemangioma of the liver associated with angiomas of the adrenals, ovaries and uterus. In Langhans's case²⁷ the hemangiomata were in the liver and spleen, and Roggenbau²⁸ describes the asso-

²⁶ Loc. cit.

²⁷ Loc. cit.

²⁸ Loc. cit.

ciation of a liver hemangioma with a hemangioma of the scrotum. Ullmann²⁹ has reported a case of liver hemangioma associated with numerous cavernoma of the skin and von Falkowski³⁰ has studied an interesting case which showed multiple bloodvessel tumors, "mesenchymal Hamartome," in the liver, spleen and skin.

Hemangiomata of the bone are uncommon tumors. Virchow³¹ described a case of hemangioma of the parietal bone associated with a liver hemangioma. Schöne³² has collected 20 cases, 7 of which were of the skull. Von Bruchanow³³ has described a case of cavernous angiomata of the liver, the skin and the periosteum of two ribs. Stamm³⁴ studied a case which presented hemangiomata in the muscles, bones, cartilage, kidneys, ovaries, small intestine, vocal cords, lungs, skull and brain. No tumors of the liver occurred in his case.

THE ADRENALS. Both adrenals were very much enlarged, of about equal size, measured 11 x 8 x 4 cm., and weighed together 350 grams. The surface was very uneven, numerous cyst-like structures were evident and here and there extensive hard, gritty areas. On puncture of these cysts a thin yellowish fluid escapes after hardening in 5 per cent. formalin. The adrenals cut with much difficulty, and on cut section (Fig. 5) there were numerous cysts present, very irregular in shape and varying in size from 5 cm. to 5 mm. in diameter. Some of these cysts were filled with a clear yellowish jelly-like material while others contained shrunken masses of dark reddish material, apparently clotted blood. In many places the walls of the cysts and the tissue between the cysts contained areas of hard, stony-like substance. These areas of calcareous material were so extensive that it was necessary to decalcify the bits of adrenal tissue that were embedded and sectioned for microscopic study.

Microscopic slides were prepared from different portions of the adrenals, frozen sections and paraffin sections being used for study. The sections were stained with hematoxylin and eosin, Van Gieson's stain and Mallory's anilin-blue stain.

The microscopic picture (Fig. 6) of the larger cysts showed the walls to be composed of a rather dense fibrous tissue, below which were areas of persistent adrenal tissue, the collections of adrenal cells

²⁹ Multiple Kavernome der Haut und der inneren Organe bei einer Frau. K. K. Gesellschaft d. Aerzte in Wien (quoted by v. Falkowski³⁰).

³⁰ Ueber eigenartige mesenchymale Hamartome in Leber und Milz neben multiplen eruptiven Angiomen der Haut bei einem Saugling, Beitr. z. path. Anat. u. z. allg. Path., 1914, lvii, 385.

³¹ Loc. cit., p. 372.

³² Ueber einen Fall von myelogenen Hemangioma des Os Occipitale, Beitr. z. path. Anat. u. z. allg. Path., 1905, VII, Supplement, p. 685.

³³ Hemangiome der Leber, Ztschr. f. Heilkunde, 1899, xx (quoted by v. Falkowski²³).

³⁴ Beitr. zur Lehre von Gefäßgeschwülsten, Inaugural Dissertation, Göttingen, 1891 (quoted by Falkowski²⁰).



FIG. 5.—Right adrenal with right kidney. Adrenal sectioned in half.



FIG. 6.—Section of adrenal cyst showing wall of cyst, also scattered collection of adrenal cells.

being pushed apart by a dilatation of the capillaries, but still staining intensely. The larger cysts, as a rule, were filled with a rather homogeneous hyalin material staining red with hematoxylin and eosin and yellow with Van Gieson's stain. Some of these masses, however, were not so homogeneous but were granular, and many of them were composed of masses of clumped red blood cells in various stages of disintegration.

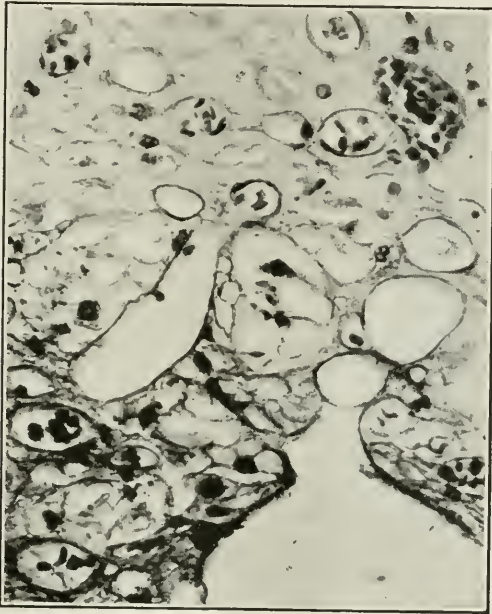


FIG. 7.—Section of adrenal showing marked dilatation of the spaces between the adrenal cells.

The microscopic picture of the tissue nearer the center (Fig. 7) showed marked dilatation of the spaces between the columns of adrenal cells. The dilatation varied from what could be interpreted as a simple dilatation of the capillaries or bloodvessels (so-called "sinusoids") to a dilatation sufficient to produce cysts smaller but similar in structure to the large ones. Some of the dilated spaces were filled with blood cells, some contained few red blood cells and others were apparently empty.

The areas of calcification were very extensive. In many places these areas were in the tissue between the cysts, in other places the cyst contents consisted of calcified material and in a few places there were definite patches of osseous tissue, with typical lacunæ and bone corpuscles.

True cysts of the adrenal are unusual. Oberndorfer³⁵ studied a case of multiple cysts in one adrenal. His specimen showed multiple lymphangiectasis of the adrenal with the formation of smaller and larger cavities and cysts. He also noted marked dilatation of the blood lymph vessels and believed a "stasis of these vessels to be the primary cause, with a resultant cystic degeneration." Sick³⁶ described a cystic adrenal formed by dilated lymph spaces in which growing lymph capillaries were present. Marchetti³⁷ studied a cystic adrenal which contained two large cysts and several smaller ones and was interpreted as a degenerative process due to abnormal secretion of the adrenal combined with destruction of the cellular elements. Henschen³⁸ described under the term "struma suprarenalis cystica hemorrhagica" a single large cyst of the adrenal containing 4000 c.c. of chocolate-brown fluid. He proposes a classification of adrenal cysts into parasitic cysts, false cysts (cystoide) and genuine cysts (cystome). A further subdivision of true cysts he makes as follows:

Cystome:

(a) Epithelial:

Follicular.

Ciliated.

(b) Endothelial:

Lymphangiectasis.

Lymphangioma.

Sick's³⁹ remarkable case of a ciliated cyst of the adrenal is the only case he found belonging to the group of ciliated epithelial cystomata. This condition he considered to be probably due to a developmental displacement of tissue from the urogenital anlage.

McCosh⁴⁰ removed a large cyst which was diagnosed as an endothelioma. Doran⁴¹ removed a large single cyst and collected 12 cases of adrenal cysts from the literature, without, however, attempting any classification of them. His specimen showed no minute cysts or lacunæ on cut section. De Vecchi,⁴² in 1910, reported what is apparently the first case of bilateral adrenal cysts recorded. He considered his case an example of a lymphangioma. His article contains a very comprehensive study of the literature on

³⁵ Lymphcysten der Nebenniere, Beitr. z. path. Anat. u. z. allg. Path., 1901, xxix, 516.

³⁶ Ueber Lymphangiome, Arch. f. path. Anat., 1903, clxxii, 459.

³⁷ Ueber eine Degenerationscyste der Nebenniere mit kompensatorischer Hypertrophie, Arch. f. path. Anat., 1903, clxxii, 472.

³⁸ Ueber struma suprarenalis cystica hemorrhagica, Beitr. z. klin. Chir., 1906, xlix, 217.

³⁹ Flimmerepithelcysten in der Nebennierenkapsel und in einer Beckenlymph drüse, Arch. f. path. Anat., 1903, clxxii, 468.

⁴⁰ Cysts of the Suprarenal Gland, Ann. Surg., 1907, xlv, 878.

⁴¹ Cystic Tumor of the Suprarenal Body Successfully Removed by Operation, British Med. Jour., 1908, i, 1558.

⁴² Ueber einen Fall doppelseitiger Nebennierenzysten, Arch. f. path. Anat., 1910, cc, 151.

this subject. Nowicki⁴³ also described a case of bilateral adrenal cysts which he regarded as lymphangiomatous in origin.

Küttner⁴⁴ described a large hemorrhagic cyst of the adrenal and collected 12 other cases from the literature. Preusse⁴⁵ reported a large lymph cyst associated with amyloid degeneration. He found evidences of proliferation of the lymph vessels and considered his case as a true example of a lymphangiomatous process.

Our case is apparently an example of the group designated by Henschen⁴⁶ as true cysts, and its appearance both grossly and microscopically resembles closely the cases considered by their authors as lymphangiomatous. The relative rarity of this condition is indicated by the figures of de Vecchi, who collected, including his own, only 9 cases from the literature, and some of them were doubtful. Nowicki added another case and Preusse reported the eleventh case. Our case is apparently the third case of bilateral cystic adrenals which has been described.

The interpretation of these cases is not altogether clear, as a review of the literature indicates. Nor are the results of the microscopic study of our case altogether satisfactory. The differences between parasitic cysts, false cysts and true cysts are sufficiently apparent, but the distinction between the epithelial and endothelial cysts in the sense of Henschen are not so clear. Some of the descriptions of the epithelial cysts resemble very closely the picture described by other observers as characteristic of the endothelial (lymph) cysts.

Furthermore, the work of Stoerk⁴⁷ casts some doubt upon the interpretation of the so-called epithelial cysts. This observer has shown that the adrenal cells form no true acini, with a central lumen which could form a "follicular" cyst as the result of distention by the secretion from the cells. In addition, the idea of an increased secretion from the cells accumulating in the center of the acini runs counter to the generally accepted view that the adrenal cells secrete into the blood stream. Nowicki⁴⁸ has substantiated the work of Stoerk.

Most of the observers who have reported lymph cysts of the adrenal have laid much stress upon the dilated spaces which are present between the columns of adrenal cells and also specially marked in the medulla of the organ. These dilated spaces have been generally interpreted as dilated lymph vessels and the process labelled lymphangiomatous.

⁴³ Zur Kenntnis der Nebennierenzysten, Arch. f. path. Anat., 1912, cvii, 338.

⁴⁴ Beitr. zur Kenntnis und Operation der Struma suprarenalis cystica hemorrhagica, Beitr. z. klin. Chir., 1913, lxxxii, 291.

⁴⁵ Ueber ein Lymphangiom einer Amyloid entarteten Nebenniere, Centralbl. f. allg. Path. u. path. Anat., 1914, xxv, 961.

⁴⁶ Loc. cit.

⁴⁷ Beitr. zur normalen Histologie der Nebennierenrinde, Berl. klin. Wehnschr., 1908, lv, 773.

⁴⁸ Loc. cit.

These dilatations, however, as enlargement of structures normally present, would necessitate for their proper interpretation an intensive study of the normal architecture of the adrenal.

Moers⁴⁹ and Joesten⁵⁰ noted in the medulla large spaces, with connective-tissue walls which were often filled with coagulated fluid. The former considered them lymph sinuses while the latter thought they perhaps had some relation to the lymphatic system. Flint,⁵¹ however, in his classic work on the adrenal, showed by injection methods that these spaces are part of the venous tree, and states that "the large lymphatic spaces described by Moers and Joesten are undoubtedly thin sections of uninjected branches of the venous tree." Also, he found that anastomoses between the veins of the medulla were uncommon and so the previously described venous plexus and sinusoids "must be regarded as a misinterpretation of the venous tree." These observations of Flint indicated clearly that all such spaces cannot at least be interpreted offhand as lymph spaces or that a dilatation of them indicates a lymphangiomatous process. That lymphatic spaces are present to some extent between the adrenal strands seems, however, to be definitely established by the injection experiments of Stilling,⁵² who also demonstrated a lymphatic net on the cortex.

In all of the sections of the adrenals in our case the degenerative changes were very striking. The fibrous tissue which formed the walls of the larger cysts showed no lining of endothelium and all presented many large irregular areas of hyaline degeneration and calcification. In many places the only tissue between the large cysts was a rather loose fibrous-like tissue which, however, showed irregular lacunæ apparently produced by softening. When stained with Mallory's anilin-blue stain this tissue stained blue, showing rather numerous strands here and there of connective tissue, which took an intense red stain. In many places also the adrenal tissue showed marked evidences of degeneration, masses of adrenal cells were in varying stages of disintegration, and these masses often had disintegrated to such an extent that there was little left but the framework of reticulum. In places where small groups of cells had perished there were small cysts formed, in other places cysts of considerable size were formed in a similar manner and in many of them fine strands of reticulum were still visible running out from the wall of the cyst toward the center but dissolving before a bridge was formed across the cyst.

The interpretation of these sections, especially in the light of their origin, is a difficult matter. Since the larger cysts were filled with a fluid closely resembling lymph it is perhaps safe to label this

⁴⁹ Quoted by Flint.⁵¹

⁵⁰ Quoted by Flint.

⁵¹ The Bloodvessels, Angiogenesis, Reticulum and Histology of the Adrenal, Johns Hopkins Hosp. Rep., 1900, ix, 153.

⁵² Zur Anatomie der Nebennieren, Arch. f. path. Anat., 1887, cix, 324.

specimen as a case of lymph cysts of the adrenal. The very prominent role played by the connective tissue in this process is in agreement with the views of Ribbert,⁵³ who has emphasized the independent growth of connective tissue in lymphangiomatous and cystic processes. The dilatation of the spaces between the otherwise normal adrenal cells is best interpreted not as a growth of lymphatic spaces resulting eventually in cyst formation but rather as a dilatation of blood and lymph circulation produced by the large cysts.

Many of the spaces and small cysts as previously mentioned were filled with blood. In some sections these pictures were so prominent as to cast a suspicion that we are actually dealing here with a hemangiomatous process. These findings, however, were not constant enough to warrant this diagnosis, but they do indicate that the bloodvessels as well as the lymphatics have played a role in the process.

A brief summary of the pathological findings in this case show:

1. A huge hemangioma of the liver weighing nearly one-half (4.9) of the entire weight of the patient. This hemangioma is a growing tumor, an example of a true hemangioblastoma.

2. Two hemangiomata of the skull, located in the temporal bones.

3. Multiple cysts of both adrenals, apparently the result of congenital disturbances of growth in which connective-tissue lymphatics and bloodvessels have all played a role. Degenerative changes are very marked.

AN OPERABLE TUMOR INVOLVING THE GASSERIAN GANGLION.

BY CHARLES H. FRAZIER, M.D., Sc.D.,

PHILADELPHIA.

MY experience with tumors of the Gasserian ganglion includes 3 of 43 recorded cases or 3 of the 13 cases in which the tumor was exposed on the operating table. The nomenclature "tumors of the Gasserian ganglion," I believe is misleading, since, as a matter of record, with few exceptions, all tumors so designated are tumors of the middle or posterior fossa, with only coincidental involvement of the ganglion and not infrequently of other contiguous nerves. With three exceptions the "tumors of the Gasserian ganglion," so called, exposed on the operating table, have been inoperable tumors of the middle fossa. Of the 3 cases in my clinic the tumor in 2 hitherto recorded (Case II and Case III) was inoperable; the third case was of interest

⁵³ Ueber Bau, Wachstum und Genese der Angiome nebst Bemerkungen über Cystenbildung, Arch. f. path. Anat., 1898, cli, 26.

for two reasons: (1) because the operation was performed within three months of the appearance of symptoms; (2) because the growth was limited in size and well within the bounds of "operability."

The patient, a man, aged fifty-three years, was admitted to my service at the University Hospital, December 22, 1916 (File No. 33568). He had been suffering for three months from pain in the distribution of the second division of the left trigeminal nerve, which was at first "jumpy" in character, later becoming more intense. This was followed by numbness in the upper lip and was associated with or followed by neuralgia above the left eye. The case was regarded as one of trigeminal neuralgia. Two successive alcoholic injections only partially relieved the pain and the patient preferred a radical operation to repeated injections.

Operation. January 8, 1917, under ether anesthesia the ganglion was approached through a butterfly incision according to my usual technic. The middle meningeal artery was exposed and divided and the foramen spinosum blocked with cotton. Upon reflecting the dura from the surface of the ganglion an almond-shaped, encapsulated growth, overlying the ganglion and appearing to take its origin from the latter structure, was revealed. There was no difficulty in separating the dura from the ganglion throughout the greater portion of its circumference, but in the neighborhood of the second division and of the sensory root the tumor was firmly adherent. In order that we might discontinue the ether and to prevent a return of pain should the tumor recur the sensory root was avulsed. The tumor was removed *in toto* and afterward the outer two-thirds of the ganglion was taken away because of the possibility of its being infiltrated with tumor cells.

The results of the operation were eminently satisfactory to the patient; his exuberance of spirit when wholly relieved of pain was a source of amusement to all who saw him in the hospital. The wound healed *per primam* and the patient was discharged eight days after the operation.

Pathological diagnosis: endothelioma. The specimen (Fig. 2) consisted of an oval, pear-shaped mass of tissue measuring 2.5 x 1 x 1 cm. At one pole the tumor measured 0.5 cm. in diameter and gradually tapered until at its expanded extremity it measured 1.3 x 1 cm. The thin upper end was dark red in color, the globular end pale white, the whole mass being firm in consistency. Section through the tumor showed a homogeneous white surface which represented the globular expansion, and this portion seemed to be circumscribed and distinct from the narrow upper pole to which it was attached. Microscopic examination disclosed a process which consisted of a fibrous connective-tissue stroma, present in a large amount, between the meshes of which appeared numerous cells. The cells varied in shape, some being spindle, others vesicular. The entire picture presented a distinctly polymorphous character. The cells took a deep nuclear stain; the protoplasm was well stained with

eosin; the cells were arranged in small clumps in many areas, occurring in the form of whorls after the manner of tumors springing from endothelium.

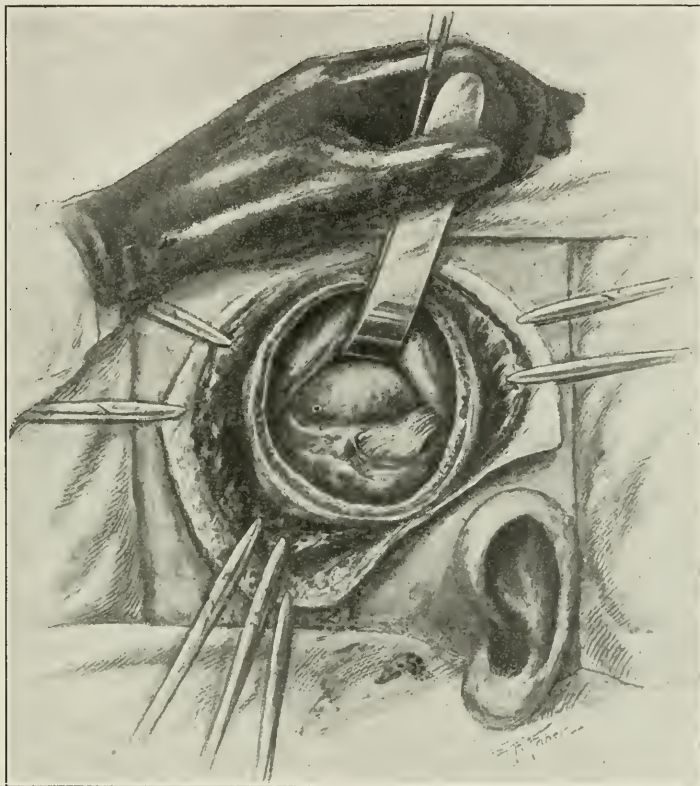


FIG. 1.—Drawing showing relation of the Gasserian ganglion to the third division and the superior surface of the ganglion, drawn in the course of the operation.



FIG. 2.—Photograph of tumor after removal.

Two of the author's cases have already been recorded by Spiller.¹ Briefly the conditions were as follows:

CASE II.—The patient, a man, aged twenty-five years, was referred to my service at the University Hospital, by Dr. William G. Spiller, April 11, 1907. In the winter previous to admission the patient suffered from paralysis of the right trigeminal nerve, accompanied by severe pain. Three months before admission the right

¹ AM. JOUR. MED. SC., 1908, cxxvi, 721.

optic nerve was seriously involved and later the left, until complete blindness resulted. There was deafness on both sides and bilateral impairment of the sense of smell; headache became most intense; the patient vomited a number of times and the left arm became paretic. The patient was unconscious upon admission. A lumbar puncture showed the cerebrospinal pressure equal to 27 mm. Hg., and 15 c.c. of cerebrospinal fluid were removed. A temporal decompression was done on each side, but the patient died within a few hours. At the autopsy a tumor measuring 4 cm. in either direction and extending 3 cm. into the brain was found growing from the dura, covering the floor of the middle fossa as far forward as the right sphenoidal fissure, also the inner part of the petrous portion of the temporal bone in the posterior fossa, extending over the basilar process as a flat growth as far as the left posterior clinoid process. The tumor was most developed at the site of the right Gasserian ganglion, which was entirely obliterated, and the right fifth, third, fourth and sixth nerves were enveloped in it.

CASE III.—The patient, a man, aged forty-three years, was referred to my service at the University Hospital March 7, 1906. He had suffered from severe pain and weakness in the distribution of the right trigeminal nerve for about five months. Hearing was impaired on the right side and the pupils were unequal and responded sluggishly to light; there was weakness of the right external rectus muscle, some retraction of the right eyeball and narrowing of the right palpebral fissure. An enlarged lymph node removed for examination revealed an endothelioma. The pain became so intense that an attempt at relief by operation seemed imperative. At the operation, April 5, 1906, I found an inoperable growth, only a portion of which was removed, but before closing the wound the sensory root was divided. The patient recovered from the operation, and until his death, two months later, the pain was bearable. At the autopsy the tumor mass was found to extend from the base of the skull into the temporal lobe, which was edematous and soft; the mass was yellowish in color and easily separable from the brain. The tumor occupied the region of the right Gasserian ganglion and not even a remnant of ganglion tissue could be seen.

While the clinical picture of tumors of the Gasserian ganglion is not always definite, nevertheless there are certain signs and symptoms which may be regarded as characteristic. The first clinical manifestations are almost invariably subjective and objective sensory disturbances in the distribution of the trigeminal nerve on the side of the lesion. Pain is usually experienced in the distribution of the three branches almost simultaneously, although occasionally, if the tumor be small and encapsulated, the pain may be limited for some time to that part of the nerve whose fibers are affected in the ganglion, as in Case I of my series. The pain, which is severe from the first, is continuous, of constantly increasing intensity, with frequent paroxysmal exacerbations. Objective sensory disturb-

ances also appear early in the same distribution, first in the form of hyperesthesia, later of hypesthesia and hypalgesia, gradually being transformed to anesthesia and analgesia. These are accompanied by trophic disturbances of the cornea, terminating in neuroparalytic keratitis and sensory disturbances in the tongue and mucous membrane of the nose on the corresponding side. The motor branch of the trigeminal becomes paralyzed sooner or later, causing paresis or paralysis of the masseters, temporals and pterygoids.

It may happen, as in Case I, that the trigeminal is the only cranial nerve implicated, but we frequently find, particularly in cases in which the tumor has assumed large dimensions, signs of oculomotor paralysis and involvement of the fourth and sixth nerves, unilateral visual disturbances on the side of the lesion, disturbances of the sense of smell and occasionally involvement of the seventh and eighth nerves. According to Spiller,² tumors of this region are prone to extend in the form of a flat growth along the base of the middle fossa, thus involving the temporal lobe without infiltrating the brain, although they may be closely adherent to it. A manifestation of this extension has been noted in disturbance of the sense of smell, but this can hardly be regarded as a regional symptom; it may be due to an extension of the growth forward or merely to the pressure incident to increased intracranial tension. Nor can the signs of increased intracranial tension in general be looked upon as significant, since they are an almost constant accompaniment of brain tumor of any locality. Paresis of the extremities has been noted in several cases and hemiplegia in one. The finding of enlarged cervical lymph nodes, emphasized by some authors, merely indicates the presence of a tumor and throws no light upon its location; it may be of use, however, in the presence of other localizing signs. Percussion of the skull has been found to be of value by several. In the case of Hofmeister and Meyer³ percussion produced severe pain in the right temporal region, and a deep tone, which was limited to a spot the size of a mark, immediately over and in front of the right auditory meatus.

STATISTICAL TABLE FROM AN ANALYSIS OF TWENTY-NINE CASES.

Age of patient.	
20 to 30 years	7
30 to 40 "	6
40 to 50 "	7
50 to 60 "	1
70 to 80 "	1
Left or right side.	
Left side	15
Right side	6
Primary, etc.	
Primary	9
Secondary	9
Doubtful	3

² Loc. cit.

³ Deutsch. Ztschr. f. Nervenheilk., 1906, xxx, 206.

REGIONAL SYMPTOMS.

1. N. trigeminus.	
Pain in trigeminal distribution	8
Hyperalgesia	1
Pain and anesthesia	4
Paresthesia	1
Anesthesia	3
Anesthesia confined to left cornea and left half of tongue	1
Loss of corneal reflex	4
2. N. oculomotor.	
Ptosis: Unilateral	3
Bilateral	2
3. N. abducens.	
Diplopia	3

NEIGHBORHOOD SYMPTOMS.

Deafness	1
Tinnitus	1
Hemiplegia	3
Paraplegia	3

SYMPTOMS OF INCREASED INTRACRANIAL TENSION.

Headache	4
Dizziness	2
Vomiting	1
Ataxia	2

It is not difficult to understand that occasionally tumors involving the Gasserian ganglion are confused with tumors of the cerebello-pontile angle, or indeed with certain inflammatory processes involving the base of the brain. The Gasserian ganglion, situated as it is in the middle fossa on the anterior surface of the petrous portion of the temporal bone and protected by its dural envelope, is seldom invaded by tumors arising in the cerebellopontile angle. Nevertheless, the root of the trigeminal nerve, as it makes its exit from the pons, may be so involved as to cause both subjective and objective sensory disturbances, which can scarcely be differentiated from those caused by implication of the ganglion itself. Although a tumor of the Gasserian ganglion may occasionally implicate the eighth nerve, deafness seldom develops until very late in the course of the disease, and only after the severe subjective and objective disturbances of the trigeminal nerve have persisted for some time. On the other hand, eighth nerve involvement is not unusual in "recess" tumors, and in "acoustic" tumors the nerve is of course uniformly involved. Of other manifestations of cerebellopontile tumors ataxia has also been observed in tumors of the Gasserian ganglion, but only in exceptional cases.

It is sometimes difficult to distinguish at first between a tumor of the Gasserian ganglion and a syphilitic or tuberculous meningitis involving the ganglion, but by appropriate examinations the presence or absence of a syphilitic or tuberculous process may be determined. Moreover, such chronic inflammatory processes develop slowly and may even completely subside for a time, while

tumors in this region usually grow rapidly and soon assume large dimensions.

The proportion of cases of trigeminal neuralgia, so called, to tumors involving the ganglion of Gasser is, in my experience, about 100 to 1; that is to say, I have seen but 3 cases of tumor to over 300 cases of neuralgia. Symptomatically, tumors of the Gasserian ganglion are, at least in the early stages, often confused with "tic douloureux." In tumors there is often a combination of pain and anesthesia; the pain more frequently involves the entire distribution of the trigeminal nerve, is of greater intensity and usually without the intervals of freedom so characteristic of trigeminal neuralgia. In tumors the corneal reflex is often absent, the muscles of mastication affected, other cranial nerves, particularly the third and sixth, are implicated, and there are the neighborhood symptoms and the signs of increased intracranial tension.

In a careful review of the literature there seem to be all told but 43 recorded cases of tumor of the Gasserian ganglion, 30 revealed at autopsy and 13 on the operating table.

CHRONOLOGICAL TABLE OF THE THIRTEEN RECORDED OPERATIONS UPON "TUMORS OF THE GASSERIAN GANGLION."

Date.	Recorder.	Operator.	No.
1895	Krogius	Krogius	1
1900	Keen	Keen	1
1906	Hofmeister	Hofmeister	1
1906	Spiller	Frazier	2
1907	Marchand	Marchand	1
1908	Giani	Durante	1
1911	Hartig	Krause	3
1913	B. Sachs	Berg	1
1916	E. Sachs	E. Sachs	1
1918	Frazier	Frazier	1
Total			13

The great majority of these 43 recorded cases have been either sarcoma or endothelioma, as will be seen in the accompanying table:

Sarcoma	15
Endothelioma	10
Carcinoma	3
Glioma	3
Gumma	2
Fibroma	1
Neurocyst	1
Aneurysm	1
No diagnosis	7
	43

According to Hellsten⁴ the ganglion possesses a peculiar resistance to the invasion of tumors. Practically all take their origin, not from the Gasserian ganglion, but from the dura or some other structure of the middle fossa and involve the ganglion only coincidentally. While at first they may be limited to the region of the ganglion, they

⁴ Deutsch. Ztschr. f. Nervenheilk., 1914, lii, 290.

expand often in the form of a flat growth along the floor of the middle fossa, occasionally invading the orbit, the sella turcica or even the posterior fossa.

Since the first operation by Krogius,⁵ in 1895, there have been reported, including my own, 13 cases of tumor of the Gasserian ganglion which have been exposed at operation; of this number 10 were large inoperable growths and the death-rate was high. In but 3 cases was the tumor operable in the sense that it could be completely removed. These were the cases of Berg, Sachs and the author. In the case of Sachs and Berg a burning sensation had been experienced eleven months prior to operation. A large endothelioma, involving the entire ganglion and all its branches, was exposed and removed. The patient made a good recovery and two months after the operation was free from pain and complained of nothing save loss of taste on the left side.

In the writer's case the operation was performed within three months of the first symptom. The patient was seen fifteen months after the operation and, apart from certain paresthesias, which might well have been due to avulsion of the sensory root, there were no signs of recurrence.

In those 3 cases in which the tumor was strictly within operable limits there were no operative fatalities. On the other hand, when a radical operation was ambitiously but unwisely attempted the results were in most instances disastrous. When the lesion has advanced beyond the point where an attempt at removal can be made with propriety one should not shrink from operation, if only as a measure of temporary relief. To this end avulsion of the sensory root for the relief of pain or subtemporal decompression for the relief of pressure may give the patient a respite for which he may be most grateful.

**SAHLI'S VOLUME SPHYGMOBOLOMETER: A RECENT
IMPROVEMENT OVER THE OLDER PRESSURE
SPHYGMOBOLOMETER.¹**

BY NATHANIEL BOWDITCH POTTER, M.D.

UNTIL 1918, PROFESSOR OF CLINICAL MEDICINE, COLUMBIA UNIVERSITY (COLLEGE OF
PHYSICIANS AND SURGEONS); VISITING PHYSICIAN TO THE NEW YORK CITY HOSPITAL;
CHIEF OF MEDICAL DEPARTMENT, ST. MARK'S HOSPITAL; CONSULTING
PHYSICIAN TO THE FRENCH HOSPITAL, THE NEW YORK THROAT, NOSE AND
LUNG HOSPITAL AND THE CENTRAL ISLIP STATE HOSPITAL; DIRECTOR
OF THE MEMORIAL LABORATORY AND CLINIC FOR THE STUDY
AND TREATMENT OF NEPHRITIS, GOUT AND DIABETES AT
SANTA BARBARA, CALIFORNIA.

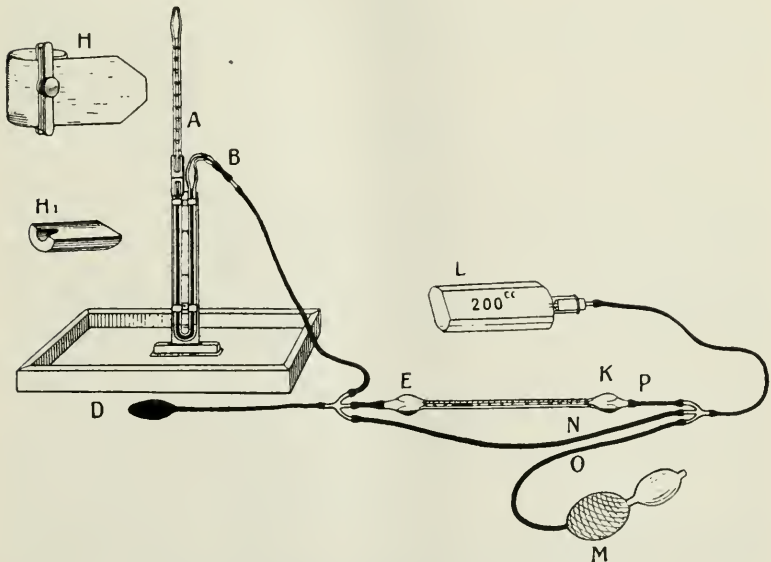
ENDEAVORING to improve the latest modification of his sphygmobolometer, to simplify the entire procedure and to further the clinical

⁵ Revue de Chir., 1896, xvi, 434.

¹ Cf. Potter, N. B.: Jour. Am. Med. Assn., April 19, 1913, p. 1211.

applicability of this dynamic method of studying the pulse, Sahli has recently introduced² the volumephygmobolometer (volumebolometer) as distinguished from the pressuresphygmobolometer (pressurebolometer). The latter directly estimates the *pulse work* (*arbeit*), whereas the new instrument measures the *pulse volume* and only indirectly, with the aid of a simple table, the *pulse work*. After many months' experience with this latest model, including a careful comparison with the former (pressurebolometer), the writer has become entirely convinced of its superiority, both in simplicity and accuracy. Many of the defects and drawbacks of the pressure instrument³ have been obviated or at least minimized, and the determination of the *pulse volume* and *work* has been made so simple that the distinguished clinician's plea for a more general utilization of the instrument and method in the study of pulse dynamics seems well worth echoing in America. It is outside the scope of this communication to discuss the clinical utility of the determinations revealed by this method, or to more than once more mention Sahli's apt contrast between them as *dynamic* and blood-pressure figures as *static* estimations, to attempt to estimate the horse-power of a locomotive from the measurement of the steam pressure in the boiler. In what follows the writer will merely describe the volumebolometer and its application, and in order to justify the entire method, enumerate a few values obtained with the old as contrasted with the new instrument.

The new apparatus, coupled together, is represented in the following cut:



² Arch. f. klin. Med., 1914, Bd. cxv.

³ Outlined in a communication to be published shortly.

It consists of two parts: Sahli's pocket mercury manometer (1914 model, *AB*), simplified by the omission of the caliber narrowing or throttling at the bend of the U-tube, and the same cuff (*H*), hard-rubber plate (*H*₁), pelotte (*D*), connecting tubing with a double rubber bulb (*M*) instead of the syringe, and a modified index manometer (*EK*). The latter, an index volumeter, alone requires description. Terminating in ampullæ open at each end (*E* and *K*) the capillary tube, with a large bore, is plainly divided into much longer subdivisions than the mercury manometer. It contains about 0.2 c.c. colored petroleum, indicating not linear centimeters but hundredths of cubic centimeters. The pelotte is applied flat and empty, as with the older instrument, and without any pressure in the system. By means of two triple Y-glass connections, and the same accurately calibrated, stiff rubber tubing (1.5 mm. in diameter), one ampulla (*E*) is coupled to the mercury manometer (*A*); to the pelotte (*B*) and with flexible tubing to its fellow ampulla (*K*); the other (*K*) to a 200 c.c. empty bottle (*L*) fitted with a perforated rubber stopper and glass tube; with soft compressible rubber tubing to a double rubber bulb (*M*) and to its fellow ampulla (*E*). Inflation of the bulb increases the system's pressure but slowly because of the inclusion of the relatively large air space in the bottle, and does not affect the position of the colored index in the capillary tube because of the free communication of the two terminating ampullæ by the compressible tube (*N*). After application of the pelotte to the radial artery in the usual way and the introduction of a sufficient pressure in the system the index will begin to pulsate as soon as this latter tube is tightly compressed by the finger of the examiner, thus excluding the large air space of the reservoir and limiting the action of the pulse to that portion of the space to the left of the index. With an open tube (*N*), tipping the index manometer will readily depress the colored index² by gravity and so enable the examiner to collect and form the index at or near the middle of the manometer. Just where this is does not matter, but if the index is too long some of the petroleum can be quickly returned to one of the two ampullæ by gravity flow, and if "split" into several indices, though this is of no special disadvantage, the superfluous smaller ones emptied into an ampulla in the same simple fashion. It is also very easy to destroy the index if it is desirable to form another. This is done by raising the manometer to a vertical or oblique position, pinching the tube (*N*) and gently pumping with the bulb. To release the pressure from the system the rubber stopper is withdrawn from the bottle, although the practically constant leaking of the bulb is usually sufficient. To avoid bursting or unduly distending the delicate rubber of the pelotte, no pressure should be exerted in the system until after the snug application of plate and cuff on the wrist. The same rules for testing the impermeability of the system as applied to the older method hold good for this apparatus, but are much less essential

because inflation of the bulb will quickly correct any leakage of air, and the results in volumebolometry are independent of the volume of the contained air.

DIRECT ESTIMATION OF THE VOLUME (V) OF THE "OPTIMAL DAMMED" PULSE (THE CLINICAL "PULSE VOLUME") (Grösse). After applying the pelotte to the radial artery, securing it in position there firmly, establishing the index and inflating with the bulb until enough pressure exists in the system to evoke a pulsation of the index, this pressure is read upon the mercury manometer. Each further increase of pressure is accompanied by pinching the two flexible rubber tubes at *N* and at *O* in order to judge the size of the pulsations of the index. If the latter is dislocated along the capillary tube a leak exists upon the side of the system toward which it moves and should be corrected. As the pressure in the system is gradually increased the pulsations lengthen, then remain for a time equal and finally diminish. The *optimal pressure* corresponds to the pressure in the mercury manometer just before which these pulsations begin to diminish again in size: in other words, the point at which the energy of the pulse beats is most completely transmitted through the system. The pulsations of the index are then read off the subdivisions of the capillary tube in hundredths of cubic centimeters. As stated above the relative position of the pulsating index in the capillary tube is of no import.

Just as with *pressurebolometry* one can advantageously control the measurement by now repeating it backward, so to speak, *i. e.*, by overstepping the point of maximum pulsation, allowing the pressure in the system to slowly decrease by means of the gradual leaking of the bulb and connections until a point is noted at which the excursions suddenly begin to once more increase. This is again the *optimal pressure*.

*These excursions at optimal pressure are an absolute measure (hundredths cubic centimeters) of the volume of the optimally dammed pulse; in other words, what we have always been accustomed to roughly estimate with the palpating finger and speak of as the size (grösse) of the pulse. This is of course merely a relative measurement of the size of the circulation based upon the pulse in that portion of the radial artery included under the inflated pelotte.*⁴ In estimating the size of the circulation, *pulse frequency* must of course be considered as well.

The detail to be remembered before reading the index is always to exclude the bulb from the system by pinching the tube at *O* as well as at *N*, otherwise the excursions would not exactly equal the volume of the dammed pulse.

Now these excursions which measure the dammed pulse are quite large and very striking, may even attain several centimeters in length,

⁴ Cf. Sahli: Deutsch. Arch. f. klin. Med., 1914, 3d exv.

and hence may be exceedingly rapid, so that sometimes an irregular movement or shaking results and produces the impression of too large a pulse volume. This is readily detected by noting that the meniscus of the index does not pause for an instant at the point at which the index is read but exhibits vibrating individual movements. To prevent this the index is shortened to 1 cm. or less by allowing part of it to flow into one of the ampullæ.

ESTIMATION OF THE PULSE WORK (ARBEIT). The *work* (*A*) is reckoned according to the following formula:

$$A = V \times P \times 13.6 \text{ gram centimeters in which:}$$

A = work,

V = volume of the dammed pulse expressed in cubic centimeters.

P = optimal pressure expressed in cubic centimeters Hg.

13.6 = specific gravity of mercury.

The accompanying table will facilitate this computation:

P. (cm. Hg.)	P. × 13.6.	P. (cm. Hg.)	P. × 13.6.	P. (cm. Hg.)	P. × 13.6.
1 . . .	13.6	11 . . .	149.6	21 . . .	285.6
2 . . .	27.2	12 . . .	163.2	22 . . .	299.2
3 . . .	40.8	13 . . .	176.8	23 . . .	312.8
4 . . .	54.4	14 . . .	190.4	24 . . .	326.4
5 . . .	68.0	15 . . .	204.0	25 . . .	340.0
6 . . .	81.6	16 . . .	217.6	26 . . .	353.6
7 . . .	95.2	17 . . .	231.2	27 . . .	367.2
8 . . .	108.8	18 . . .	244.8	28 . . .	380.8
9 . . .	122.4	19 . . .	258.4	29 . . .	394.4
10 . . .	136.0	20 . . .	272.0	30 . . .	408.0

THE SUPERIORITY OF VOLUMEBOLOMETRY TO PRESSUREBLOMETRY. As contrasted with the pressurebolometric equations the barometric pressure is entirely disregarded in volumebolometry, an advantage when employing this clinical method at elevations above 3000 feet. Another advantage is that the values are much less dependent upon an optimal application of the cuff, since in virtue of the large air space the increase of pressure in the system to produce the pulsations is a minimal one. It is advisable, however, even with this method, to secure an optimal cuff application, but this is accomplished by comparatively moderate tension of the cuff.

THE DIAGNOSIS OF CHRONIC APPENDICITIS.¹

BY WILLIAM FITCH CHENEY, M.D.,

CLINICAL PROFESSOR OF MEDICINE, STANFORD UNIVERSITY MEDICAL SCHOOL,
SAN FRANCISCO, CALIFORNIA.

THE recognition of chronic appendicitis presents many difficulties: on the one hand because its own manifestations are so variable,

¹ Read before the Nevada State Medical Society, at Reno, Nevada.

and on the other hand because so many conditions simulate it. Every patient seeking advice for stomach trouble or indigestion or abdominal pain may have chronic appendicitis as a cause while many that complain of ailments more remote, such as recurring headaches, failure to gain in weight, persistent vague symptoms, such as lack of energy and incapacity for exertion, may really owe their ill health to chronic appendicitis, as shown by their return to normal after a diseased appendix has been removed. But disease of the gall-bladder, of the ovary or the Fallopian tube or of the kidney may each produce symptoms so much like those of chronic appendicitis that to escape error in diagnosis requires the utmost care. From all sides, therefore, we are beset by difficulties, and the greater the experience the greater the caution about reaching a conclusion. Although this subject has been discussed so extensively during the past decade that not much new remains to be said, nevertheless a consideration of problems as actually presented in every-day work may be of value, because they will serve to show by what methods we decide that a diseased appendix produces the symptoms for which the patient seeks advice.

How frequently is chronic appendicitis a factor in ill-health? Probably not so often as many are ready to believe. Among 2116 medical cases seen in private practice during the five years from January 1, 1912, to January 1, 1917, only 71 after careful study presented evidence sufficiently definite so that a diagnosis of chronic appendicitis could conscientiously be made. During this same period 297 cases of chronic gastric disease were seen and 62 of chronic gall-bladder disease. The conclusion has thus gradually been reached that chronic appendicitis is too often suspected as an adequate explanation for obscure digestive ailments—much more often than is justified by the fact. There is too great a tendency to convict the appendix without sufficient evidence and to advise its removal on the basis that it is a useless organ anyway, and taking it out can do no harm. Unfortunately it is also true that in many cases taking it out can do no good.

I. HISTORY. As a means of diagnosis a careful history is always of the highest value, and it is worth while to note of what these chronic appendicitis cases complain. Of the 71 observed, 31 sought advice for "stomach trouble," 25 for pain in the abdomen, 4 for persistent abdominal soreness and tenderness, 1 for "gas in the bowels," but 7 complained chiefly of recurring headaches and 3 of lack of energy and vitality.

Stomach Trouble. Unfortunately the stomach symptoms are not always the same, so that no conclusion can be reached from this part of the story alone. Some of the cases resemble gastric ulcer in their chronicity and periodicity; with gastric attacks lasting for weeks or months, followed by days, weeks or months of remission or complete intermission of symptoms; and in the character of their

symptoms, with burning pain in the epigastrium or right or left hypochondrium as the chief complaint, this pain coming on one to four hours after eating, accompanied by belching, waterbrash and nausea. This group is found, as will be shown later, to have a reflex hyperchlorhydria as the cause of their gastric suffering. A smaller group of cases resembles chronic gastritis, with distress soon after taking food, a sense of fulness and distention but not of pain, much belching of gas and frequently regurgitation of a mouthful of food, this process going on over and over after each meal. This group shows on analysis a subacidity, but in some there must be the added factor of pylorospasm, reflex from the diseased appendix.

The history of these cases taken by itself may create suspicion of the appendix, but that is all; other symptoms and other evidence must be sought for in various ways to be described before reasonable certainty can be reached. The difficulty is that the patient's complaint about the stomach is frequently so loud and persistent that it leads the physician himself astray, directing all his attention to this organ instead of to the one really diseased.

Pain in the Abdomen. Twenty-five patients who came for advice about this symptom were found to belong in the group of chronic appendicitis. In some the pain was definitely referred to the right lower quadrant, present constantly or in spells; in others it was not so well defined but referred simply to the abdomen or to the bowels. Sometimes complaint was made also of tenderness and soreness, increased by jarring or jolting, as by riding on horseback or in an automobile. This pain was variously described as an ache, a hurting, a sense of distention or simply as soreness. It might be very annoying for days and then for days might practically disappear. In every instance this had gone on so for months or for years. Such a story, while in no way diagnostic, is extremely suggestive, and no one hearing it would probably fail to think of chronic appendicitis as a likely cause. The same is true of the four other histories in which abdominal soreness and tenderness were the chief complaints. Different patients express their discomfort in different ways, but with all these variations of the story of persistent abdominal pain and soreness the appendix as a cause should be given almost the first thought.

Symptoms Outside the Abdomen. When the patient's story is of trouble in the abdomen it is not likely the appendix would be forgotten in the search for an explanation. But 7 in the group here reviewed sought advice especially for recurring headaches and 3 for lack of energy and vitality. With such complaints, chronic appendicitis would scarcely be suspected; and yet these and other symptoms in remote parts of the body may result as the chief manifestation. The explanation perhaps lies in the associated constipation due to adhesions, with resultant auto-intoxication; but

whatever the relation may be the fact remains that in certain of these cases to be reported, removal of a diseased appendix has relieved these remote symptoms after other methods of treatment had failed.

Constipation. As regards this symptom it is too common an ailment to have any significance in relation to chronic appendicitis. The two conditions are often associated, but the question then is which preceded, which is cause and which effect. It is also being discovered gradually, as roentgen-ray plates are being made more frequently, that both the constipation and the chronic appendicitis may be secondary to prolapse of the cecum and colon and consequent stasis of contents. Chronic constipation may be due to mechanical difficulties produced by adhesions about a chronically inflamed appendix, but may be due, and probably more often is, to other factors entirely, which have likewise caused the appendix to become diseased.

Previous Acute Attacks. In any history of chronic digestive ailment a question of great importance is whether there have ever been attacks of pain in the abdomen that might have been due to acute inflammation of the appendix. These attacks may have occurred long before the patient comes for advice and may be forgotten unless sought for or they may occur from time to time simply as subacute exacerbations of the chronic disturbance or there may have been one or two previous attacks not recognized as appendicitis but called "ptomain poisoning," inflammation of the bowels, or simply "colic," and never given a thought in connection with the subsequent chronic disturbance of digestion. Such a history of previous acute attacks could be elicited in 37 of the 71 cases in this group, but not in the other 34. The significant fact lies in the absence of any such history, for it suggests that chronic appendicitis may be chronic from the beginning and that an acute onset of any sort is not essential to establish the diagnosis.

In general there is no type of history from which alone a diagnosis can be reached. Sometimes one complaint and sometimes another predominates, and sometimes there is a mixture of all those described. But other and more definite evidence must be obtained before suspicion becomes conviction.

II. PHYSICAL SIGNS. The evidence found on abdominal palpation to prove that chronic appendicitis exists may be very definite or very indefinite, very extensive or very slight. A palpable mass in the appendix area, varying in size or shape, like a thumb or a hen's egg or a sausage, with more or less tenderness on pressure—these are the expected findings. But experience teaches that these signs are very variable. No mass at all may be palpable, but the patient complains of intense pain when pressure is made over the usual appendix site; rigidity and muscle spasm may be present in the right lower quadrant of so great degree as to make localization

of any mass beneath impossible; or no mass or tenderness whatever may be found at one time of examination, though both may be present at another time. As is also well known the greatest tenderness may be found high up along the ascending colon, prompting one to suspect the gall-bladder; or low down in the inguinal region, leading in female patients to the conclusion that the disease is pelvic. Among the 71 patients whose histories have been reviewed, 62 presented definite physical signs in the appendix area, but 9 presented no evidence that could be interpreted to mean chronic inflammation there. Of these 9 patients, 6 proved at operation and 1 at autopsy to have chronic appendicitis. The other 2 have never yet had operation so far as can be traced. The diagnosis was made in these cases, and operation was advised on other data to be described as we proceed; but the point to be emphasized at this time is that absence of the signs usually expected on palpation of the right lower quadrant does not prove the absence of chronic appendix inflammation.

There are several explanations to account for this failure to find what ought to be found: (1) When the appendix lies behind the cecum, firmly attached to it by adhesions, one has to palpate not only through the abdominal wall but through the cecum in order to feel what lies beneath, and this is usually impossible; (2) one of the most troublesome forms of chronic appendicitis, so far as reflex symptoms are concerned, is the atrophic or obliterative type, where repeated disease has caused the appendix to shrivel and become buried in adhesions so that no mass exists to palpate; (3) the appendix inflammation when examination is made may be so quiescent that it gives no local evidence, even though reflex symptoms in the stomach or elsewhere persist and are very annoying; but sooner or later an exacerbation occurs and then the local signs become perfectly definite.

The lesson taught by these records is clearly that no one factor in the diagnosis is conclusive. Physical examination gives accurate information more frequently than does history alone, and the two together make us more certain than either one can by itself. But it is necessary to get together all the evidence by every possible method of investigation before we can reach anything like absolute certainty.

III. GASTRIC ANALYSIS. In the cases with gastric symptoms predominant one must investigate the stomach secretions, as a routine part of the examination, in order to reach a diagnosis. This was done in 39 of these patients, and in 28 hyperchlorhydria was found. In 1 the total acidity was 96, in 4 between 80 and 90, in 5 between 70 and 80, in 13 between 60 and 70, in 5 between 50 and 60. In 8 the secretion was practically normal, with total acidity 40 to 50, and in 3 it was subnormal, or below 40, with 1 case under 10. It is evident there is no diagnostic analysis to indicate chronic appen-

ditis, though the most common finding is a hyperchlorhydria. But if this finding happens to coincide with negative and dubious physical signs about the appendix, it is more likely to be attributed to some other cause, as ulcer, and so may be a hindrance rather than an aid to diagnosis.

IV. RADIOGRAPHIC EXAMINATION. The value of this method in recognizing chronic appendicitis has not been generally accepted and is still in question, and the experts themselves differ as to just what findings shall be interpreted to mean a diseased appendix. Nevertheless, it seems certain that as every case suspected should be given the benefit of every possible method of investigation, roentgen-ray examination can no longer be omitted. During the past year this conviction has been adopted and acted upon, and with increasing experience in the study of plates of the cecum and appendix no one can doubt the value of them or would be satisfied to give an opinion without their assistance in reaching it.

To begin with, the radiographic examination is at least eliminative of gastric conditions that confuse the diagnosis. History and gastric analysis may point direct to ulcer of the pylorus or duodenum; but if the antrum, pylorus and cap are normal on the plates the diagnosis of ulcer is evidently dubious. No patient should ever be advised to undergo operation for ulcer unless roentgen-ray plates have first been made. The only exceptions to this rule are the emergency cases, in which recent hemorrhage or continued vomiting preclude the administration of barium mixtures or when it is imperative there should be no delay. Some of the chronic appendix cases in this group of 71 were victims of a mistaken diagnosis, because in the earlier years recorded no roentgen-ray plates had been made, and only at operation advised for ulcer was it discovered that no ulcer existed but a chronic inflammation of the appendix.

But direct evidence as well as indirect can be obtained from the plates. What one may expect to find is epitomized thus by Case:² (1) poor drainage; (2) localized tenderness on acute palpation done under fluorescent guidance; (3) kinking; (4) irregularities in the lumen; (5) unduly long or large appendix. Most observers agree that long delay in emptying, with retention of opaque material in the appendix after it has disappeared from the cecum, means poor drainage due to inflamed walls, and can be depended upon as a sign of great significance.

It is admitted that a diseased appendix may fail to show on the plate because it is postcecal and obscured by the opaque material in the cecum; or because it is obliterated and cannot fill; so that negative evidence does not become a bar to the diagnosis in the face of a definite history and physical signs. But localized tenderness under the fluoroscopic screen, kinking, irregularities in lumen,

² Interstate Med. Jour., April, 1917, p. 339.

such as clubbing, long delay in emptying, with evidence of adhesions to the bowel, all constitute positive proof of abnormality that add much to the clinical picture. The only danger is that this method of examination will be accepted by the lazy man as a short cut to diagnosis, to the exclusion of other and older methods, such as a detailed history, careful palpation of the abdomen and gastric analyses. The value of radiographic examination is great in the diagnosis of chronic appendicitis, and no investigation at the present day is complete without it; but it is only a part and can never become the whole.

V. OPERATION. This method is not advised for diagnosis, but after diagnosis has been made it has been found a valuable method for revision. Out of the 71 cases in this group, operation was done on only 32 under direct observation here or as reported by the operator to whom they were referred. Others undoubtedly came to operation, but no record is at hand of what was found. The most valuable lessons have been learned from these operated cases, not so much by confirmation of conditions as predicted, but more by the additional information thus acquired, at times different entirely from what had been expected. A review of some of these cases will best serve to call attention to routine methods of diagnosis, to some of the common errors and to the problems presented in differential diagnosis.

1. *Obvious Cases.* A certain number of these patients present an easily recognized typical picture that can scarcely be mistaken, and of such the following is an instance.

CASE HISTORY. A man, aged thirty years, first seen in October, 1912, sought advice for "stomach trouble." He had been annoyed at intervals for two years, his attacks coming once a month or once in two months and lasting about a week. At these times he complained of burning pain in his right side, at the edge of the ribs, appearing two to four hours after meals, with belching, nausea and heartburn. In addition to this story about his stomach he had another, of an attack in August, 1910, characterized by cramps in the abdomen and diarrhea, lasting for two days, and two months later of a similar attack, with much abdominal pain. Four months after that he began to have more constant pain in the right side of his abdomen, with tenderness to touch; and ever since he had had this pain more or less persistently. Any jarring or jolting, as in riding horseback, would start the pain. Once he had such a severe attack of this pain that he had to quit work and go to bed. This patient's stomach showed a hyperchlorhydria, with total acidity 60, free HCl 28, combined HCl 24; and he had in his appendix area a mass the size of a hen's egg, very tender on manipulation. Operation at the time was declined and for a year he tried to get along with diet, laxatives, olive oil and alkalies. But he did not improve, and finally was operated on in December, 1913, when an extensively

inflamed appendix was removed. After that his symptoms all disappeared.

If all cases presented symptoms and signs like the foregoing one would seldom have any difficulty in recognizing their meaning, but many variations from this type occur. Perhaps the greatest difficulty of all arises when stomach complaints predominate and any history or physical signs pointing to appendix disease are for a long time lacking. The following case histories bring this out.

2. *Unexplained Gastric Cases.* A man, aged twenty-eight years, seen in January, 1915, complained only of stomach trouble, which had existed for four years intermittently. There were intervals when his stomach seemed perfectly normal. His spells varied in duration, averaging several weeks, but had gradually become more frequent. At these times he had good appetite, but soon after eating gas formed, his stomach seemed to swell, he belched much gas and had a dull pain over his stomach. Eating the next meal relieved for about an hour, then the trouble began again. His bowels were obstinately constipated, but no history could be elicited of any attacks that could be interpreted as acute appendicitis nor of any pain in the appendix area. The stomach showed hyperchlorhydria, in explanation of his symptoms, but there were absolutely no signs in the right lower quadrant that could be taken to mean a diseased appendix. A few months later, however, in April, 1915, he had a sudden attack of acute purulent appendicitis, necessitating immediate operation, when it was found that an old chronic inflammation had long preceded the acute attack.

A large fat man seen in February, 1914, said his stomach had troubled him constantly for the past five or six years. He had no appetite at all; as soon as he ate he felt like vomiting; at least once every day he did vomit what he had eaten at the previous meal; he often felt nauseated on first rising, before taking any food; and when he did not get rid of a meal, felt he would be better if it was out, because it caused so much heaviness and distress, with belching of gas. This patient was obstinately constipated and never had a movement without physic. Recently he had noted some feeling of fulness in the right side of his abdomen if his bowels did not move, but never had any severe pain there. Palpation showed tenderness on deep pressure over the appendix, but no mass of any kind could be felt. The stomach contents contained an abundance of thick ropy mucus and showed a hyperchlorhydria, with total acidity 70, free HCl 50 and combined HCl 10. The only definite findings were gastric, with nothing to justify a diagnosis of chronic appendicitis, even though it was suspected. This patient's symptoms persisted in spite of treatment, until finally he had an acute attack of appendicitis in July, 1914, necessitating immediate operation, which showed an appendix kinked and bound down by many old adhesions. After its removal the gastric symptoms all disappeared.

A girl, aged sixteen years, seen in October, 1915, sought advice for stomach trouble of long duration, with severe headaches, dizziness and lack of energy. A year before she had her tonsils removed and a bony growth from her nose, because she was told the operation would restore her health, but it did no good. She continued to complain that everything she ate disagreed and gave her pain in her left side under the ribs. These pains came on about a half-hour after eating, especially after eating sour food, such as tomatoes or fruits. She had headaches almost all the time, with dizziness, and her bowels were always constipated. Her stomach showed a hyperchlorhydria, with total acidity 64, free HCl 20 and combined HCl 32. At this time she had no complaint to make of her abdomen, and examination gave no evidence of appendix inflammation. But she continued to be troubled by sour stomach in spite of diet and laxatives, and the following December complained for the first time of pains lower down in the bowels on the right side. Finally, early in January, she had an acute attack of appendicitis, necessitating immediate operation, and this showed old chronic adhesions, indicating that the recent attack was not the first.

In all three of these cases whose histories have been related, roentgen-ray plates of stomach and intestines would have thrown light on the real pathology present, and would have aided in reaching a correct diagnosis before the final acute attack. In all such unexplained gastric cases there is a cause, and even though no appendix evidence is found at one examination it may appear at another, while roentgen-ray plates may show trouble with the appendix even when physical examination is dubious.

3. *Cases Simulating Ulcer.* In still another group of cases the clinical history and the stomach analysis appear to speak so positively for gastric or duodenal ulcer, while the physical examination of the appendix region is persistently negative, that the case seems too clear for doubt. Here again error can now be avoided by roentgen-ray plates, but this was not appreciated in the earlier years that this report covers. Instances of such wrongly diagnosed cases are the following:

A physician, aged thirty-six years, who consulted me in February, 1914, had suffered ever since he was eighteen years from severe attacks called "gastralgia," characterized by heartburn, waterbrash, sour stomach and gas. He was always thin, slender and neurasthenic. His stomach would have periods of improvement, then again would relapse, and during all these years he had never been entirely free of his indigestion. At the time he sought advice he had suffered, especially for six weeks, with pain coming on several hours after food, particularly at night, so severe he could not sleep; also heartburn, sour regurgitations, belching of gas and nausea. Physical examination showed rigidity and tenseness of the abdominal wall over the upper half, more in the right hypochondrium than

elsewhere; great tenderness there on pressure, which increased his pain; but no tenderness or rigidity elsewhere. Stomach analyses made repeatedly throughout twelve years previous to his consulting me, as well as at this time, showed always a high-grade hyperchlorhydria. Operation advised for duodenal ulcer proved conclusively there was no ulcer in either the duodenum or the stomach, but a chronic appendicitis was found, of obliterative type, with the remains of the appendix very small, hard and fibrous and buried in a mass of adhesions. After its removal he had no further dyspepsia. Within a year he gained forty pounds in weight and correspondingly in energy and efficiency.

A man, aged forty years, also seen in February, 1914, complained of stomach trouble for years past: soreness over the stomach, recurring "bilious spells," with ravenous hunger, pain over one eye, sick stomach and vomiting, and at all times weakness of digestion. He had had also repeated spells during the previous five years, characterized by severe pain in the pit of the stomach coming on before meals and relieved by eating; such spells lasted several months at a time, with intervals for months when there was no pain at all. He always had a ravenous appetite, ate very heartily, but was hungry again in three or four hours, no matter how much he ate. This man was another tall, slender, lanky individual, with a loud succussion splash and considerable tenderness over his stomach, but positively no palpable mass or tenderness over his appendix area. His stomach contents showed an excessive hyperchlorhydria, the total acidity 90, the free HCl 40 and the combined HCl 20. Operation was advised for ulcer and was performed, but no ulcer of stomach or duodenum was found. The appendix was then investigated and found to be bound down and kinked, with many old adhesions about it—a typical chronic inflammation of long standing.

Both of the foregoing cases would now be recognized before operation by negative radiographic plates of the stomach and the duodenum and by more or less positive findings about the cecum and appendix. As stated previously, and now emphasized again, no operation for ulcer is in these days justifiable unless roentgen-ray plates have first been made and studied.

4. *Cases Simulating Gall-bladder Disease.* These cases offer one of the most difficult problems in diagnosis, and not unfrequently the correct solution is found only at the operating table. Many such errors have been made in the past and they will continue to be made in the future, though probably less frequently as fluoroscopic and radiographic examinations are employed more often. Both conditions give rise to recurring attacks of abdominal pain, with intervals of good health between. Ordinarily we depend upon the site of pain and tenderness and the direction of radiation of pain to distinguish one from the other. But an inflamed appendix pointing upward along the ascending colon may cause the greatest pain and

tenderness just below the costal margin, while the pain of biliary colic may be referred downward into the right lower quadrant instead of backward under the shoulder-blade. Either attack may make its onset with chill, followed by fever and leukocytosis; either may be accompanied by vomiting; either may be followed by transient jaundice; and either condition may give rise to reflex gastric symptoms between the acute attacks. Three cases in this group of 71 were wrongly diagnosed as gall-bladder disease, and only at operation was it discovered that the real disease was chronic appendicitis. But none of these had been given the benefit of roentgen-ray examination or the error might have been avoided.

5. *Pelvic Disease Simulating Chronic Appendicitis.* In female patients the question frequently arises whether the symptom-complex is due to disease in the appendix or in the right broad ligament, for a diseased appendix pointing downward toward the pelvic brim may cause constant pain and tenderness low down, just above Poupart's ligament, while an inflamed ovary or tube may refer its pain upward into the right lower quadrant. The following case history illustrates the difficulty in these cases about reaching a correct decision:

A woman, aged twenty-four years, seen in March, 1912, complained of attacks of stomach trouble at intervals for ten years past, the last one persisting for a year. During these she had much gas and belching after food and an unnatural, craving appetite, not long satisfied; also much nausea on waking in the morning and often during the day, coming on several hours after eating, though she never vomited. All these stomach symptoms were worse during her menstrual period. She had no pain in the stomach but had experienced several attacks of pain lower down in the abdomen. Her bowels were habitually constipated. Examination revealed slight thickening in the appendix area, but no tenderness or definite mass. Pelvic examination was negative. Stomach analysis showed a hyperchlorhydria, with total acidity 70, free HCl 20, combined HCl 30. The patient's gastric symptoms were all easily explained by her hyperchlorhydria, but the absence of gastric pain from the history and of tenderness over the stomach practically excluded ulcer, while the recurring attacks of pain in the lower abdomen, the chronic constipation and the at least suspicious findings in the appendix area were interpreted to mean chronic appendicitis, to which the hyperchlorhydria was secondary. Operation, however, revealed only slight congestion of the appendix and no evidence of previous inflammation sufficient to explain the symptoms, while an ovarian cyst was found on the right side, the size of a walnut. No other pathology was discovered. Both the appendix and the cyst were removed and the stomach trouble subsequently disappeared altogether.

Naturally the most important evidence of pelvic disease is found

by vaginal examination. But this is not always conclusive. In the first place, when the anatomical changes are slight, they may be missed unless the examination is made under an anesthetic and muscle spasm thus eliminated. In another instance the appendix itself, inflamed and tender, may hang down over the brim of the pelvis, be felt on vaginal examination and wrongly interpreted as a diseased Fallopian tube. Thirdly, it is not at all uncommon to find at operation both the appendix and the Fallopian tube diseased when only one has been recognized by previous examination. Thus errors not uncommonly occur. Either condition gives rise to long-standing pain and soreness in the right lower quadrant, with recurring acute attacks when these symptoms are greatly increased in intensity, and either may cause reflexly persistent disturbance of digestion, with hyperchlorhydria.

6. *Kidney Stone Simulating Chronic Appendicitis.* This condition is mentioned as a possibility in differential diagnosis, but it has never led to error in the cases under review. The particular source of trouble is the stone escaped from the right kidney and lodged in the ureter, causing pain and tenderness and recurring attacks of colic in the right side of the abdomen in the appendix area. But aside from the evidence afforded by a careful history, bringing out the fact of radiation of pain to the bladder or to the genitalia at some time during its exacerbations, with symptoms of urinary disturbance; aside also from negative findings on palpation over the appendix; there is the positive evidence afforded by urine analysis, disclosing pus and blood corpuscles in the sediment; and the final and unmistakable proof afforded by cystoscopy, ureteral catheterization, pyelography and roentgen-ray plates.

7. *Recurring Headaches Due to Chronic Appendicitis.* Seven patients presented themselves for recurring headaches who were found to have a diseased appendix as the only adequate explanation. These cases could be best set down as "gastric headaches," but their stomach disturbance was obviously reflex from some disease outside the stomach itself. The complaint of "sick headaches" is a common one. Frequently these headaches are found to be associated with some fault in the stomach's functions and disappear after this fault is corrected. But in a small proportion the condition underlying both the headaches and the gastric disturbance can be found in chronic appendicitis. The following is an instance of the part the appendix may play.

A man, aged forty years, sought advice in December, 1916, for headaches recurring at intervals for a number of years past, and persisting in spite of glasses worn for three years continuously, fitted to overcome eye-strain. The pain in his head gradually had grown more and more constant, at times becoming so severe he could scarcely bear it. This pain was felt sometimes through the temples, sometimes through the back of his head, sometimes all

over the top. He complained also of chronic constipation, but had a good appetite and no digestive distress. He also complained, but only when asked directly about it, of a pain in the right side of his abdomen; usually only a sense of heaviness, as if there was a big lump there; but at times this became severe pain. This man was very large and heavy. He had no evidence of nephritis, a blood-pressure within normal limits and a negative Wassermann reaction. His stomach contents showed only a slight subacidity after a test meal. In the right lower quadrant was found a very definite tender mass in the appendix area, the size of a hen's egg, constantly present at several different examinations on different days. Radiographic plates showed filling defects in the cecum and ascending colon and no barium could be caused to enter the appendix. At operation, in July, 1917, the appendix was found kinked at its base, hypertrophied and elongated, with numerous old adhesions binding it down. After its removal the pain in the head, previously constant, entirely disappeared, though medical treatment of all kinds had failed to relieve it. No attempt is made to explain how the inflamed appendix caused the headaches, but the fact remains that one disappeared with the other.

8. *Neurasthenia Due to Chronic Appendicitis.* Finally in 3 of the cases included in the group here reviewed the sole complaint was of lack of energy and vitality, and the patient's story corresponded to the condition commonly called "neurasthenia." The diagnosis of an inflamed appendix was arrived at only after routine investigation in an effort to discover why the symptoms had arisen. One of these histories will suffice to demonstrate that such a relationship may exist.

A patient, aged thirty-seven years, seen in September, 1916, complained of congestion in his head, inability to apply himself to his work, insomnia, great restlessness and general "nervous breakdown." He was a large, well-nourished man, apparently in good health, but had been compelled to give up his work as a clergyman because of his symptoms. No abnormality was found in any organ on physical examination and the stomach contents showed a normal analysis after a test-meal. No cause could be found for his symptoms except a chronic constipation. A series of roentgen-ray plates, however, made of the gastro-intestinal tract showed that the appendix filled readily with bismuth but did not empty again, retaining the bismuth even after seventy-two hours. In spite of this finding, as no evidence of chronic appendicitis could be discovered on physical examination repeatedly made, the radiographic evidence was for the time disregarded. But finally, as no improvement resulted from any treatment given and as the patient remained incapacitated for his work, removal of the appendix was advised. This was done in May, 1917. The appendix and the head of the colon were found bound down by very old and very dense adhesions. The

appendix was sharply angulated at its base, close to the bowel, and its distal portion distended and thickened. After removal of the appendix this patient made a prompt convalescence. He rapidly recovered his usual energy and desire for work, went back to it in July and is now apparently as active and vigorous as ever before in his life. Nevertheless, this case does not prove that neurasthenia is always or often due to chronic appendicitis but only that it may be in exceptional instances.

The object of all diagnosis is rational treatment, and once chronic appendicitis is diagnosed there is no cure but surgery. We wish therefore to be very certain before we advise; certain that this condition exists; certain that it is responsible for the ill health of which the patient complains; and reasonably certain that removal of the diseased appendix will restore good health. These considerations have prompted this review of the methods by which we reach a decision and of the other possibilities that must be remembered before we select the appendix as the proper point of attack.

**MULTIPLE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S
DISEASE) AND ITS INHERITANCE: WITH
DESCRIPTION OF A CASE.**

BY SAMUEL A. PREISER, M.D.,

MEDICAL SERVICE OF MONTEFIORE HOME AND HOSPITAL, NEW YORK,

AND

CHARLES B. DAVENPORT,

CARNEGIE INSTITUTION OF WASHINGTON; EUGENICS RECORD OFFICE, COLD SPRING
HARBOR, N. Y.

1. CLASSICAL SYMPTOMS OF MULTIPLE NEUROFIBROMATOSIS. Among the rarest of abnormal conditions of the surface of the body is that characterized by a large number of sessile or pedunculated swellings or tumors, sometimes soft and elastic, sometimes firm and tough, that vary in size from that of a millet-seed to that of a child's head. The skin over the tumors is frequently discolored, brownish or bluish, or reddish through enlarged capillaries. They may be present from birth and they may tend to grow, usually very slowly, but they rarely, if ever, regress in size. When numerous and large in one area they may become confluent. Examination shows that they are fibrous tumors, frequently containing one or more nerve fibers; or, when more deep-seated, being enlargements of the perineurium of the nerve trunks. They are due to localized cell proliferation of the connective-tissue sheaths of the nerves.

Metabolic changes frequently influence the course of the disease. The changes or pregnancy are stimulative. Thus in Meek's(1905) case "the first nodule appeared on the right shoulder during her (the propositus's) first pregnancy and steadily increased in size. During each succeeding pregnancy (but never in the interim) new growths appeared." In Hirst's(1911) case the patient (who was at the time of examination aged thirty-eight years and had numerous tumors) married at twenty-five years and became pregnant at twenty-six years. Up to this time she had only four or five tumors which had first appeared at eighteen years; during the first pregnancy they increased greatly in number.

The changes of puberty are apt to be associated with the first marked development of the tumors. In Arnozan and Prioleu's (1883) case the patient's sister noticed her tumors increasing in size after puberty, just as one of the patient's had. In Rapok's (1890) patient, a girl, aged seventeen years, the tumor of the eyelid had grown rapidly during the preceding one and a half years; note also Hirst's(1911) case. Likewise in Laignel-Lavastiné et Leroy's (1905) case the generalized tumor formation was first noticed in the female patient at eighteen years. In Czerny's(1874) history the patient's mother had a tumor in the region of the upper thoracic vertebræ, and this began to grow rapidly at twenty-six years, after her menses had, precociously, ceased.

The exciting role of various infections is somewhat supported by many reported cases. Marie(1903) laid great stress on this point. In one of the cases reported by Fraenkel and Hunt(1903) the tumors developed after typhoid fever. Rolleston(1899) reported a case in which, after an attack of pneumonia, the tumors became more numerous. Rolleston and MacNaughton(1912) reported the occurrence of the disease after the injection of diphtheria antitoxin in two sisters whose father was also a victim of the disease. Intoxication may also be an etiological factor. Tumor growth has been observed after arsenical intoxication. Our case had an attack of lead poisoning before the disease developed. An attempt has been made to connect von Recklinghausen's disease with tuberculosis. Cases in which the two conditions were associated have been recorded by Poncet(1909), Mosse(1907-8), Pic and Rebatu(1908), Pic and Gautier(1908) and Oulmont and Haller(1909). One of von Recklinghausen's patients died from hemoptysis after admission to the hospital, and at the autopsy cavities were found in the lungs together with tuberculosis of the kidneys and intestines. The case to be reported here had an old pulmonary tuberculosis. Caution has to be exercised in drawing conclusions from this association, however, since tuberculosis is so common a disease.

Frequently associated with the tendency to form tumors is another—namely, the production of pigmented spots or patches

in the skin. These, likewise, may be present from birth, but more commonly they are first noticed later. The largest may be several decimeters in diameter. The usual color is *café au lait*. The pigment spots are not unrelated causally to the tumors. Nevi or pigmented spots frequently arise first as colored moles or small tumors, which flatten out to form *café au lait* patches. The same tendencies that cause proliferation of the cells of the derma also cause a special proliferation of the pigment cells of that tissue.

Incidental to the tendency to form tumors we find a variety of other conditions which are occasionally present. These will be considered in Section 3.

Painful symptoms due to the disease are either entirely absent or they correspond more or less to those of neuralgia or neuritis. The neurofibromata may remain latent and may be first accidentally discovered during an examination, or, as in one of the cases reported by Fraenkel and Hunt(1903), revealed only at autopsy. In some cases these tumors manifest themselves by intense pain, which arises at the site of the tumors and radiates in the direction of the nerves. There is also a great tenderness on pressure. As a rule there is paresthesia, sometimes hypesthesia, in the area of distribution of the affected nerve, but rarely paralysis or atrophy. Reflex local muscular contractions may also develop, and even general convulsions of the type of reflex epilepsy. The disease had been observed in connection with epilepsy, hysterical hypochondriasis and neurasthenia, and is occasionally accompanied by sensory disturbances and mental disorders. Gastric disturbances have been noted in cases of von Recklinghausen's disease, and it is of interest that in one of these cases miliary fibromata were found postmortem in the wall of the stomach and duodenum.

The number of these nodules varies with age and constitution of the individual. They tend to increase in number, as well as in size, with age. At one extreme there may be only a solitary growth upon one nerve, at the other the number is very great. Thus, Robert Smith(1849) counted 450 on one limb and over 2000 on the whole body. Octerlong(1875) counted 2333 tumors on a negress of sixty-six years and the count did not include some of the smaller ones. But the record of patience in counting seems to be held by Hashimoto(1890), who made out 4503 tumors on the skin of a middle-aged Japanese man.

2. DISTRIBUTION OF NERVE TUMORS. The distribution of nerve tumors on the body offers some matters of interest, especially in respect to symmetry and relation to particular nerves.

(a) *Symmetry*. Since the nerves of the body are symmetrically placed we might expect to find some symmetry in the distribution of nerve tumors, and such is often the case. Some authors specifically refer to such symmetry. For example, Speransky(1895) says the pea-sized tumors had a rather symmetrical distribution.

Sequeira(1916) states that his girl patient had symmetrical, bright red lesions on each side of the nose.

(b) *Distribution of Tumors among the Different Nerves.* The frequency with which the different nerves are mentioned in the reports might be expected to yield some facts of interest. But it has to be recognized that certain parts of the body are more apt to be seen and reported upon than others, because more accessible. Bearing this in mind the relative order of frequency with which particular nerves are mentioned is about as follows: ulnar, radial, orbital nerves, nerves of buttocks, sciatic and crural nerves. The various plexuses and the cranial nerves are often mentioned, but, on the other hand, the tumors are less common on the palmar surfaces of the hands and feet.

3. SYMPTOMS SOMETIMES ASSOCIATED WITH MULTIPLE NEUROFIBROMATOSIS. (a) *Scoliosis.* This is frequently mentioned, for example, by Genersich(1870), Speransky(1895), Antelme(1897), Adrian(1902), Lion and Gasne(1904), Chiray and Coryllos(1905), Hintz(1909), Oulmont et Haller(1909), Cole and Shawan(1911), Vignolo-Lutati(1911) and Rolleston and MacNaughton(1912). Sometimes the result is due to the formation of tumors on spinal nerves near their roots. Thus intervertebral ligaments are stretched and the vertebral column distorted.

In the half-brother of Genersich's case (who also showed neurofibromatosis) the dorsal and lumbar regions of the spine were strongly bent backward and a little to the right without a compensatory forward bend. In Antelme's case there was a tumor on the left arm of such weight as to cause the patient's head and shoulder to bend toward the left and the thorax and even the spine and sternum to curve in. In Adrian's case a tumor on the right scapular region, of the size of the child's head, was removed at twenty-six years, and during the subsequent thirty years there had been a slowly increasing deformity of the spine and thorax. In Lion and Gasne's case a woman, aged forty-four years, who shows a few rather large tumors, has the thorax and vertebral column deformed in the sense of a dorsal kyphoscoliosis, with slight lumbar lordosis. In Chiray and Coryllos's case a man, aged thirty-seven years, who was improperly nourished in infancy, has now numerous fibromata and a very accentuated kyphoscoliosis. Eight of his 10 sibs died of meningitis in infancy. In Hintz's case a boy, aged five years, with numerous small swellings, a slight scoliosis, had been discovered at three years. In Oulmont and Haller's case a man, aged forty-nine years, had shown tumors since his tenth year, and they were now numerous and large. He was undeveloped mentally and sexually and showed a facial asymmetry and a slight scoliosis. In Cole and Shawan's case there are large tumors and a markedly deformed spine, but in this case there was a history of an injury

by being thrown from a wagon at twelve years. In Vignolo-Lutati's Case II the male patient, aged fifty-seven years, showed numerous small hard tumors, a slight lumbar scoliosis and a slight alveolar prognathism. In Rolleston and MacNaughton's case a girl, aged thirteen years, with incipient molluscous tumors, there was a slight scoliosis.

In considering these cases one must not forget that a slight scoliosis is rather common in the population at large, due to a variety of causes. Nevertheless, the relation of such scoliosis to tumors is in some cases (like Antelme's) direct and mechanical, in other cases probably due to less obvious relations to the formation of nerve tumors, such as swellings on the roots of the spinal nerves.

(b) *Sexual Impotence.* This is referred to, for the male, in several instances; for example, Hashimoto(1890), Chiray and Coryllos(1905), Deumié et Monéry(1908), Oulmont et Haller(1909) and Vignolo-Lutati(1911). The significance of this matter is not perfectly clear.

(c) *Feeble-mindedness.* While it is true that fibromatosis may occur in families showing the best of intellectual development, yet it is also true that the amount of feeble-minded among those who are affected with multiple neurofibromatosis is strikingly large. Of 243 persons described in the literature examined by us having multiple tumors, 19 were feeble-minded, or 7.8 per cent., or say twenty times the frequency found in the population at large.

4. IMMEDIATE CAUSES STIMULATING THE DEVELOPMENT OF THE TUMORS. It is often stated that the tumors develop in response to special stimuli. Thus in Labourverie's(1899) case the patient was a gendarme. The author states: "Irritation from sword-belt clothes, etc., and injuries have certainly contributed to the increase of certain tumors on the waist and back." A neuroma on the sciatic nerve is attributed to a strain resulting from jumping a ditch. However, one must not lay too much stress on these "explanations." Though tumors are frequent on the buttocks they are relatively rare on palms and soles. They sometimes arise about the region of the hat brim, but they also occur on the face, nose, jaw, popliteal space and in the nerves of the plexuses and the body cavity, where their development cannot be ascribed to special pressures. Very frequently they are numerous on the surface of the body before birth. No doubt pressure irritates tumors as they begin to form, but it is not the primary cause of tumor formation, and, indeed, it has little modifying effect.

5. LAW OF RECURRENCE OF NEUROFIBROMATOSIS IN THE FAMILIES. Multiple neurofibromatosis is a rare condition, as it is found in only about 1 in 2000 cases that present themselves to medical clinics or private practitioners for skin diseases. No doubt there are many abortive cases which never get into the literature, but,

even so, the proportion of the population which has the classical symptoms of neurofibromatosis is very small. Despite this there are many cases in the literature of two to six members of a family—blood relatives—who show some of the symptoms. Of such families the pedigrees of some are presented in Figs. 1 to 34. The frequent concurrence of these relatively rare symptoms in several

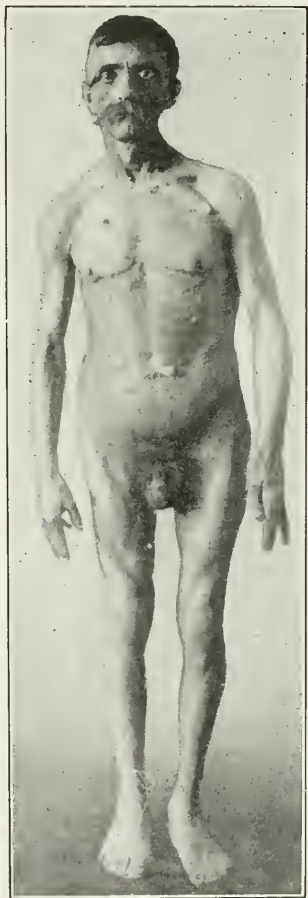


FIG. 1.—Front view of patient, M. G.



FIG. 2.—Rear view of patient, M. G.

members of one family cannot be accidental. It must be due either to the presence in the family of internal factors tending to induce the symptoms or to external agencies (such as contamination, germinal infection) which act upon individuals (like those of a family) who are in intimate contact. The fact that only *blood* relatives are affected speaks strongly against the contact hypothesis. The possibility of an infection through the germ cells cannot be

denied. It is to be noted, however, that father and child are quite as often affected in the same way as mother and child. This proves that the tumors do not belong to the class of diseases that are induced merely by infection through the placenta.

Though so many cases are on record of more than one affected person in a family, it is not to be overlooked that in very many reports no mention is made of relatives who have similar symptoms

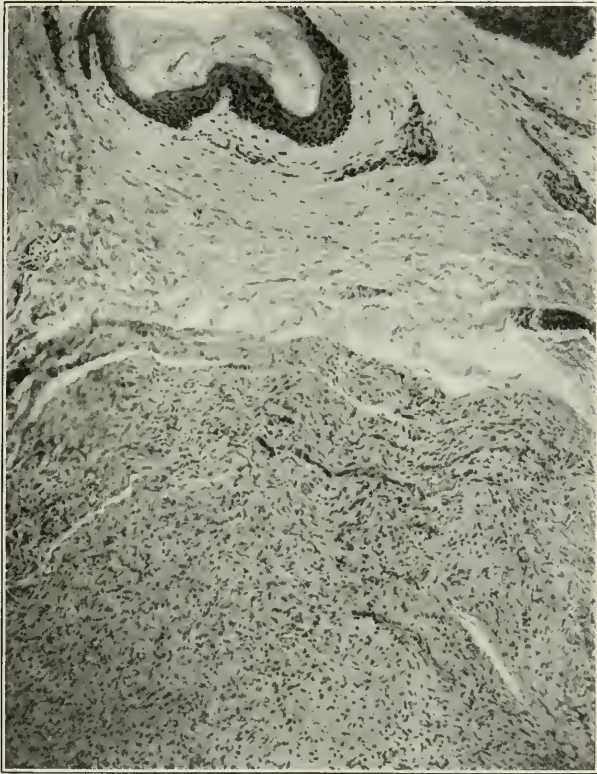


FIG. 3.—Photomicrograph of section of characteristic neurofibroma in deeper layer of dermis taken from trunk. Magnification, 300 diameters.

with the patient; also, there are a number of cases in which the existence of affected relatives was denied. The charts given are of those of families in which there were two or more affected persons in one family. They represent only a few of the examples of such families studied by us in the literature.

In considering the nature of the family distribution we have first to recognize that the two sexes are apt to be affected in approximately equal numbers. Thus of the 243 persons described in the

literature examined as having multiple tumors there are 138 males and 105 females, or 56.79 per cent. males.

The disease tends to recur without a break in the generations, and it is nearly equally apt to be the case that the father or the mother of the patient is affected, whether that patient be male or female. Thus in the families charted we find that in the case of 119 males it is the father who is affected in 49 cases, the mother in 46 cases and neither parent is recorded as affected in 24 cases. In the case of

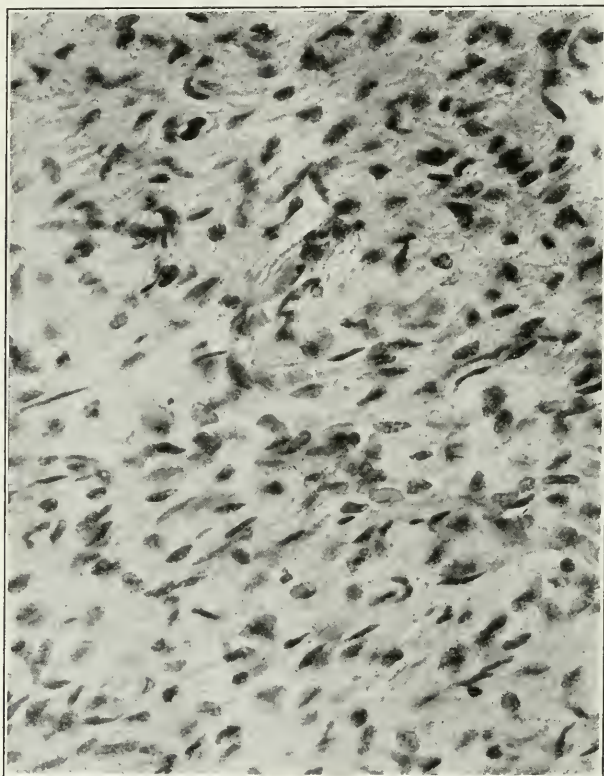


FIG. 4.—Same as Fig. 3, high power. Magnification, 700 diameters.

72 females the father is affected in 29 cases, the mother in 34 cases and neither parent is recorded as affected in 10 cases. We can here see no evidence of a difference in the distribution of the disease in the sexes when the father, on the one hand, or the mother on the other, is the affected parent.

In so many instances do the symptoms reappear in the direct line of ancestry that the hypothesis is at once suggested that the hereditary factor in neurofibromatosis is a dominant one. On this hypo-

thesis there is something in the germ plasm that positively facilitates the production, under appropriate stimulation, of tumors of the nerve sheaths.

On the hypothesis that neurofibromatosis depends on a dominant factor we should expect ordinarily half of the offspring of an affected parent to show the trait. Considering in the pedigree charts Nos. 7, 8, 10, 11, 12, 17, 18, 19, 21, 23, 24, 25, 26, 27, 29, 30, 31, 32, 33, 34 the fraternities with 2 or more offspring of an affected parent



FIG. 5.—Section of neurofibroma showing extensive degeneration. Magnification, 300 diameters.

we find (Table I) of 115 such offspring that 50 are affected. This is 43.5 per cent., approaching the 50 per cent. expected if there is a dominant factor for neurofibromatosis.

An apparent difficulty in the way of hypothesis that multiple neurofibromatosis is a dominant trait seems to lie in the fact that breaks in generations actually do occur. That "no family history" of a direct ancestor is obtained in response to the usual superficial inquiries made by the practitioner of hospital cases is not surprising;

the fact that a disease like his own occurs in other members of the family is apt to be denied (if indeed recalled) by the patient under the stressful conditions of the examination; the patient often exhibits the reactions of the malingerer. In a few histories like that of Fig. 29, II, 2, it seems probable that a generation is actually skipped. This is by no means fatal to the view that the disease depends upon a dominant trait, for a precisely similar result is obtained in experimental breeding of clear dominant traits, *e. g.*, in polydactylism of fowl. Occasionally a dominant trait simply fails of expression in an individual who carries it.

TABLE I.—PROPORTION OF FRATERNITY AFFECTED WITH NEUROFIBROMATOSIS.

No.	Total.	Affected.	No.	Total.	Affected.
7	2	2	26	2	2
8	7	2	27	8	1
10	4	3	29	8	3
11	2	2	29	5	2
12	11	1	29	6	1
17	6	4	29	3	0
18	2	2	30	3	1
19	3	1	31	5	5
21	4	3	31	5	0
21	2	1	32	2	1
23	3	3	33	5	1
24	3	1	33	7	3
25	3	1	34	4	4
			Totals		
			115 50		

6. SPECIAL FAMILY TYPES. In examining comparatively the symptoms shown by different patients one finds a great diversity in them, and also that the special symptoms exhibited in one member of the family are very like those shown in another member. The resemblances relate to the region preëminently affected, to the nature of the tumors, to the time of their development and so on. Let us consider some examples of these family resemblances in symptoms.

(a) *Family Resemblances in Location of Principal Tumors.* Since in most cases the tumors are exceedingly numerous it is to be expected that they will sometimes occur in different members of the family in corresponding parts of the body. But, apart from this, we have instances in which single exceptional tumors appear in exactly corresponding places, and this frequency must be regarded as significant. Some of these instances are here cited from the appendix.

Bruns(1870). The patient was born with a flat tumor of the left temple and left upper eyelid which grew with the growth of his body into a lobed sac hanging over the (not atrophied) eyeball. His brother had a tumor of the temporal region and the left upper

eyelid almost exactly like that of his brother, and which grew in the same way.

Genersich(1870). The patient has numerous small tumors, but on the upper part of the right buttock there is a soft lipoma the size of two fists. His half-brother had at ten weeks before his death a tumor the size of a fist in the deep part of the buttock. It grew very rapidly and at the time of his death was seventeen inches in circumference.

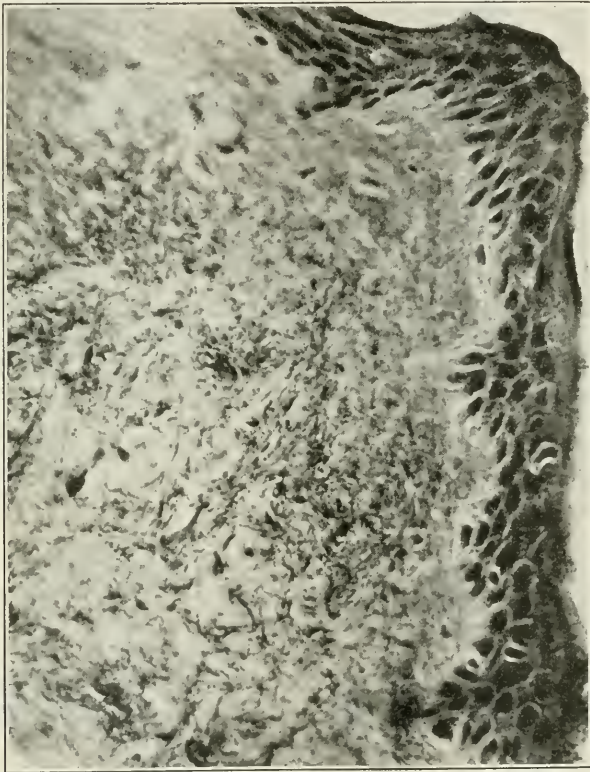


FIG. 6.—Same as Fig. 5, high power. Magnification, 700 diameters.

Murray(1873). In the patient, aged seven years, the last phalanx of the fingers, with one exception, and several of the toes, were hypertrophied to from three to four times their natural size. A four-year old sib had the end of one of the fingers similarly enlarged. In the patient the gums were greatly hypertrophied, covering up almost entirely the teeth. The two younger sibs presented the enlarged gums.

Czerny(1874). The patient is said to have been born with a

small swelling on the back; at six years a physician certified that it was as large as a fist; at twenty-five years it hung down so far, starting from the region of the lowest thoracic vertebræ, that she

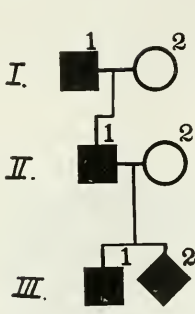


FIG. 7

FIG. 7.—Case of R. Virchow, 1847. III 1, patient had numerous knotty soft fibroid tumors. III 2, similarly affected sibs; number and sex unknown. II 1, similarly affected father. I 1, similarly affected grandfather.

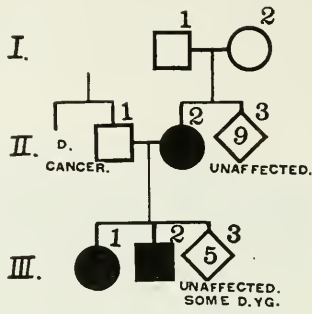


FIG. 8

FIG. 8.—Case of A. Hitchcock, 1862. III 2, propositus, aged forty-six years, showed numerous small pedunculated skin tumors; a large one of twenty years' standing lay on the ulnar nerve; this returned after removal. III 1, a sister, began to have tumors at ten years. After removal of tumors numerous others arose. II 1, had brothers and cousins who died of cancer. II 2, at eighty-one, had hundreds of tumors, which grew slowly in number and size; she denies that her sibs or parents had tumors.

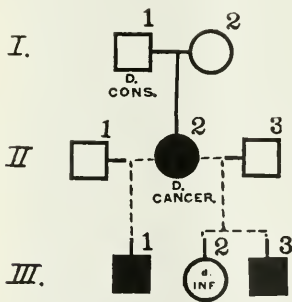


FIG. 9

FIG. 9.—Case of A. Genersich, 1870. III 1, a day laborer, aged thirty-four years, showed numerous hard and soft skin tumors; on autopsy many fusiform tumors were found upon the nerves. III 3, a half-brother, showed numerous resistant, fusiform tumors which were first noticed at eight years; on autopsy fibromata and also sarcomata were found on numerous nerves. II 2, died of cancer of the breast; she had small cancers on nerve trunks.

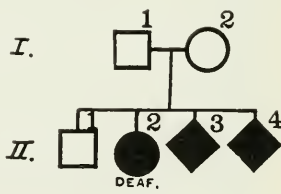


FIG. 10

FIG. 10.—Case of J. Murray, 1873. II 2, aged seven years, showed a variety of cutaneous growths; some of the tumors grew again after removal. II 3, 4, children of four and two years, who show beginnings of tumors. I 1, 2, first cousins; showed no tumors.

was obliged to give up her field work. Her mother had a tumor in the region of the upper thoracic vertebræ like that of her daughter; when it was extirpated it weighed 38 pounds. The

mother's brother had a tumor on his back which hung down so as almost to prevent his walking; the mother's father had a similar

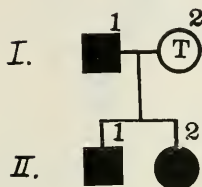


FIG. 11

FIG. 11.—Case of J. E. Atkinson, 1875. II 1, Timothy Lyons, aged fifty-six years, shows multitudes of small tumors, some 5 cm. in diameter; has large pigmented nevi verrucosi. II 2, aged fifty years, fewer tumors than brother, with a tendency to pedunculation; present since infancy. I 1, had numerous tumors; one "weighed two pounds."

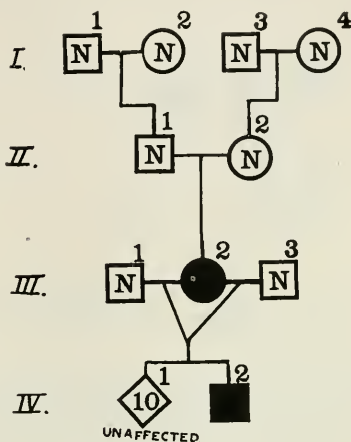


FIG. 12

FIG. 12.—Case of Oeterlony, 1875. III 2, patient, a negress, aged sixty-six years, showed 2333 skin fibroid tumors of varied size and consistency. IV 2, of eleven children, one at twenty-two years, had numerous tumors. II 1, 2, parents, as well as grandparents, said to be unaffected.

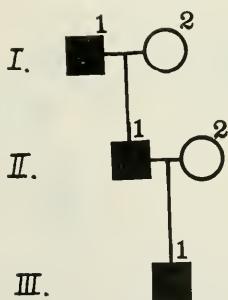


FIG. 13

FIG. 13.—Case 1 of T. Fox and T. Farquhar, 1876. III 1, a Brahmin, aged thirty-three years, showed from adolescence numerous small skin tumors, now of varied size and consistency. II 1, at sixteen years, began to show numerous small skin tumors. II 2, unaffected. I 1, had numerous tumors, mostly about the size of a pea.

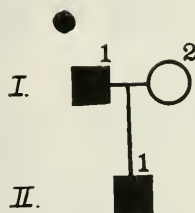


FIG. 14

FIG. 14.—Case 6 of Fox and Farquhar, 1876. II 1, aged sixty years, has had body studded with tumors from childhood if not from birth; one is now as large as an orange and cystic in consistency. I 1, similarly affected.

huge swelling on his left arm. The mother's father's brother had a swelling on his back which hung far down and almost prevented

his walking. Thus in three generations there was the tendency to form a huge tumor, usually on the thoracic vertebrae.

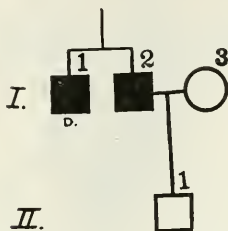


FIG. 15

FIG. 15.—Case of Fox and Farquhar, 1876. I 2, a Mohammedan coolie, aged forty-five years, shows numerous sessile tumors of various sizes. His son, II 1, aged thirteen years, is still free from tumors. I 1, affected like his brother; his parents unknown.

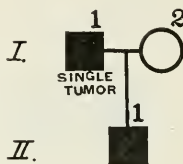


FIG. 16

FIG. 16.—Case 8 of Fox and Farquhar, 1876. II 1, an East Indian boatman, aged thirty-five years, had tumors from childhood, which constantly increased in number and size. A huge tumor, which felt like a half-filled bladder, was excised, but after eighteen months grew more rapidly than ever. I 1, had a single tumor over the left shoulder-blade.

Herczel(1890). After describing in detail the distribution of tumors in the patient, states of the mother, who had tumors also, that “these growths are in exactly the same places as in the daughter.”

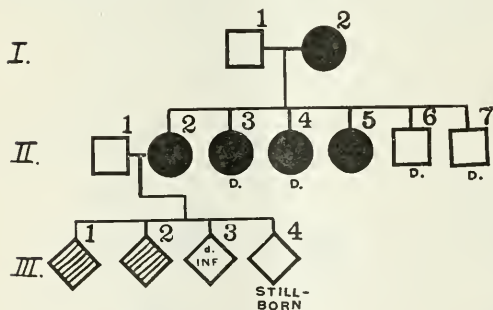


FIG. 17

FIG. 17.—Case of Konigsdorf, 1899. II 2, aged forty-five years, showed over 600 skin tumors of varied size, with golden pigment spots and increasing scoliois. Autopsy revealed numerous soft fibromata of the skin, throat and liver, fibrosis of the dura mater and lipoma of the left kidney. II 3, 5, three sisters had tumors like her own. I 2, had tumors like the patient's.

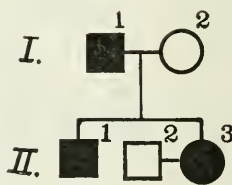


FIG. 18

FIG. 18.—Case of Hashimoto, 1890. II 1, a Japanese, aged forty-two years, was born with skin tumors which have increased in number to 4503, of varied size; the skin is also pigmented. II 3, has fibromata over her whole body. I 1, had numerous skin tumors.

Moses(1890) records the case of a man with multiple tumors that produced an elephantiasis. The mother had the same affection of soft multiple fibromatosis and elephantiasis as the son.

In Rapok's(1890) case, father and daughter had a plexiform neuroma. In Phillipson's(1893) case, mother and mother's mother had a fibroma in the inguinal furrow, and the daughter had one in

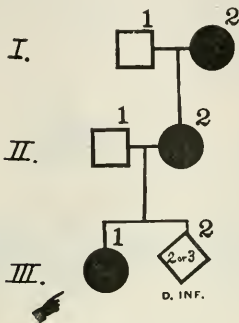


FIG. 19

FIG. 19.—Case of J. C. Gilchrist, 1896. III 1, aged twenty-six years, has had tumors all her life; shows a violaceous patch and a telangiectatic spot. Five days after removal a tumor was replaced by a sarcomatous growth. II 2, died at twenty-five years, with an enormous number of tumors, some of great size, one of which developed into a cancer. I 2, affected like III 1.

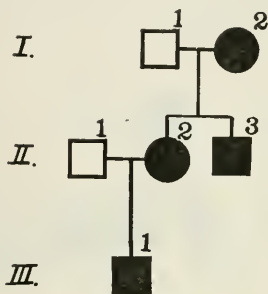


FIG. 20

FIG. 20.—Case of W. Menke, 1898. III 1, aged twenty-three years, shows innumerable pigment spots and numerous neurofibromata. II 2, has neuroma; a large one in the same place as her son's large tumor. II 3, had numerous small tumors on his arms from birth. I 2, had small nodules along the nerve tracts of all extremities.

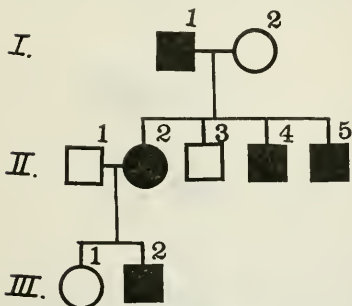


FIG. 21

FIG. 21.—Case of T. Carwardine, 1899. III 2, aged twenty-five years, was covered with nodules of varied size, some deep-seated, and a pendulous fibroma upon one buttock. Several pigment patches and a multitude of freckles. II 2, similarly affected. II 4, 5, similarly affected. I 1, similarly affected.

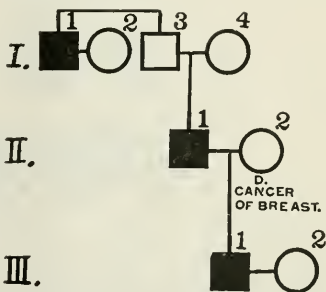


FIG. 22

FIG. 22.—Case of J. Labouverie, 1899. III 1, gendarme, aged thirty-four years, shows numerous brown punctiform spots; four cutaneous fibromata, a molluscum fibrosum and a molluscum pendulum on the back. Tumors at the waist exaggerated by sword-belt. II 1, aged fifty-six years, showed patches and numerous fibromata of the nerves. I 1, aged eighty-eight years, showed pigment patches and molluscous tumors.

the "genital region." Gilchrist(1896) reports on the similarity of the growths in daughter, mother and mother's mother. Tailhefer (1897) emphasizes the similarity of the tumors in the patient, her

sister and father; and Spillman et Etienne(1898) find similar or exactly similar tumors in son, mother and mother's father. Bourcy and Laignel-Lavastine(1900) find three generations of scalp tumors.

In Malherbe's(1901) case, mother and daughter had exactly similar tumors on the left breast. In Menke's(1898) case the tumors in three generations are large ones on the median nerve; in

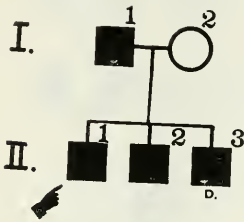


FIG. 23

FIG. 23.—Case of B. G. A. Moynihan, 1901. II 1, aged thirty-seven years, showed whole body covered with small tumors, some sessile and some pedunculate. Irregular pigment patches were shown which, like the excrescences, were present at birth. One tumor, taken from the vagus, proved to be a neurofibroma. II 2, 3, covered with brown patches and soft excrescences. I 1, like his sons, covered with patches and soft excrescences.

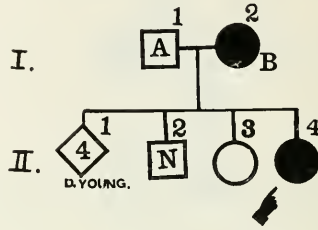


FIG. 24

FIG. 24.—Case of C. Adrian, 1902. II 4, was subject to cutaneous tumors from birth on. At fifty-six years they were very numerous, sessite and pedunculate; brown skin patches were present. On autopsy neurofibroma were found on the viscera. I 2, had numerous tumors over the surface of the body; became blind, "B."

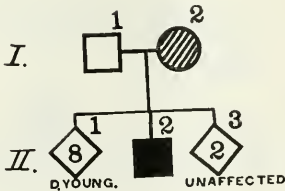


FIG. 25

FIG. 25.—Case of Chiray and Coryllos, 1905. II 2, aged thirty-seven years, showed pigmented spots from birth; tumors from twenty years. Fibromata are specially marked on superficial nerves of the appendages. I 2, has pigmentation like son, but no tumors.

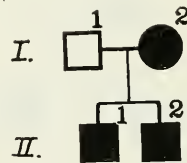


FIG. 26

FIG. 26.—Case of C. R. Keyser, 1905. II 1, aged thirty-eight years, shows numerous painless skin tumors gradually becoming more numerous; there are large pigmented areas. II 2, even more markedly affected by multiple tumors. I 2, said to have died of tumors which formed a large growth extending across her chest.

Thomson's(1900) case one of the striking tumors occurs in father and son on the buttocks; in de Haam's(1912) case there are two generations of swelling over the eye. In Lange's(1906) case the family showed a stronger tendency to form pigment patches than tumors, while in other cases no pigment patches are seen. In Du Bois's(1917) case mother and daughter had a large tumor arising from below the left breast.

The foregoing examples illustrate the conclusion that not only is there a general tendency to multiple tumors in the family but also a tendency to produce them of the same type and in the same places.

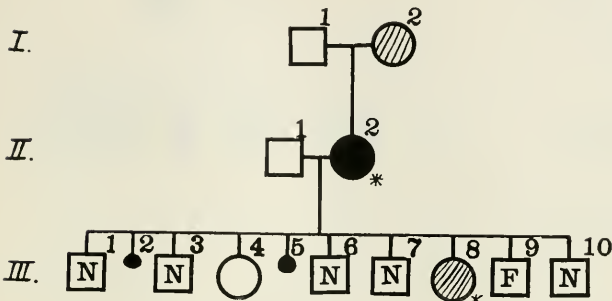


FIG. 27.

FIG. 27.—Case of E. B. Meek, 1905. II 2, aged forty years, shows numerous subcuticular nodules which are painful; also pigment spots. The optic nerve is beginning to atrophy. III 8, shows numerous pigment spots but no tumors. I 2, had pigment spots in the skin. *Individuals seen by Meek.

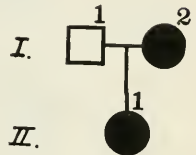


FIG. 28.

FIG. 28.—Case 1 of F. Harbitz, 1909. I 2, aged fifty-two years, showed numerous fibromata and pigment spots. II 1, aged twenty-three years, showed pigment spots, angiomata and soft fibromata.

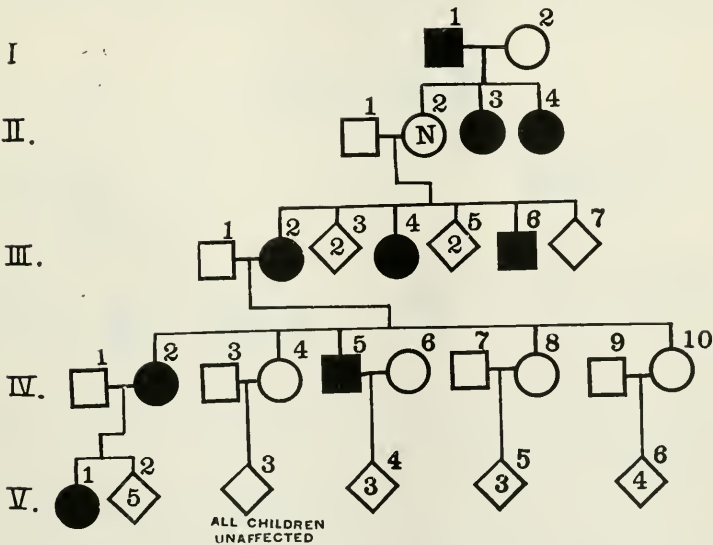


FIG. 29.—Case 9 of F. Harbitz, 1909. V 1, aged twenty-five years, showed "elephantiasis" of the left leg, due to confluence of fibromata. Similar "elephantiasis" had existed in other members of the family, as shown on the chart.

(b) *Family Resemblances in the Associated Symptoms.* Inside a particular family the symptoms often show special idiosyncrasies. The behavior of the pigmentation in families is peculiar. Some-

times it will be only the pigmentation changes that are shown by a young child of an affected person; in such a case one suspects that

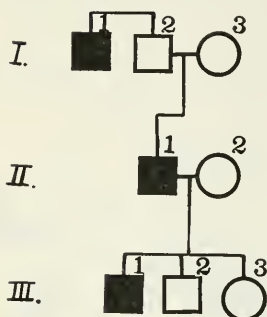


FIG. 30

FIG. 30.—Case of A. Hintz, 1909. III 1, aged five years, showed numerous gold-brown flecks and numerous little swellings beneath the skin. III 2, showed a red mark on the body. II 1, aged forty-two years, showed small skin tumors by the thousand; some sessile and some pedunculate. He had also flecks of pigment. I 1, had skin changes like his nephew.

FIG. 31.—Case of H. M. Cole and H. Shawan, 1911. II 1, aged forty years, showed multiple subcutaneous tumors from boyhood; the skin shows pigment blotches. II 3-6, all have multiple skin tumors. I 2, had a round painless tumor removed from her arm; no multiple subcutaneous tumors.

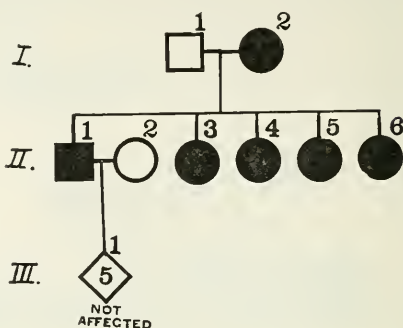


FIG. 31

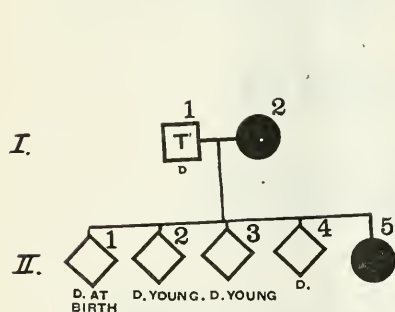


FIG. 32

FIG. 32.—Case of W. B. Trimble, 1911. I 2, aged forty-seven years, was practically covered with small fibrous tumors, varying in size and color; also with areas of skin pigmentation. II 5, aged nineteen years, has small tumors on her arm which first appeared at sixteen years.

FIG. 33.—Case of A. Mathies, 1913. II 2, aged thirty-five years, died blind and deaf. Autopsy showed numerous tumors along peripheral nerves, tumor of the orbit, knots at base of the brain, tumor of optic chiasma and visceral nerves. III 1, aged fifteen years, blind and deaf on left side, numerous tumors along peripheral nerves. III 2, aged thirteen years, undeveloped, tumor of the twelfth cranial nerve on a cutaneous posterior femoralis. III 4, aged twelve years, undeveloped, many tumors on arm.

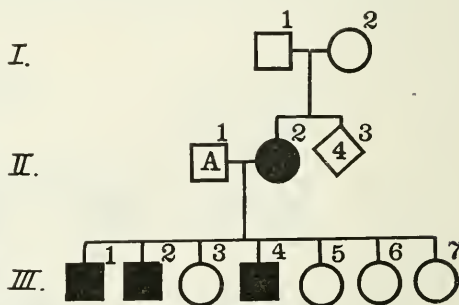


FIG. 33

the tumors will appear later. In other cases, however, the parent of an affected person may show pigment only—no tumors. However, in many cases the pigment relations are similar in various

members of the family. For example, extensive pigmentation of patient and mother is noted in the Herczel(1890) case. In Salomon's(1878) case the small coffee-colored flecks were alike in brother and sister. Spillman et Etiene(1898) report a case with pigment patches in two generations and one case without patches in two generations. Sutherland(1906) reports similar pigment spots in three generations.

The size of the tumors is usually variable. Frequently a single or a few large tumors appear. There is a notable case described by Czerny(1874), such as one might doubt if we had to do with multiple fibromatosis were there not numerous small tumors, though no pigment changes. On the other hand in not a few families, such as those of Fox and Farquhar(1876), the tumors are all small.

A tendency to produce the rather uncommon *confluent tumors* (elephantiasis) also runs in families. In Moses's(1890) case mother and son showed "elephantiasis." In Harbitz's(1909) case No. 2 elephantiasis appeared in five generations.

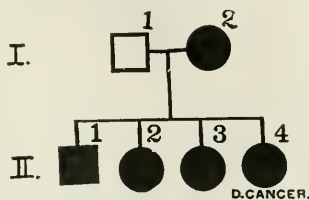


FIG. 34.—Case of Billington, 1914. II 1, aged thirty-seven years, showed superficial tumors all over the body from childhood. II 2, 3, had many subcutaneous tumors. II 4, had growths all over the body; died of cancer. I 2, had a tumor on the right arm.

Finally, though the tumors are usually benign, yet in some families they tend to *develop into sarcomata*. For example, in Arnozan and Prioleau's(1883) case a tumor in the patient was tending into a sarcoma and a sister's large tumor was sarcomatous. In Genersich's(1870) family some of Karl's tumors were distinctly sarcomatous and in his mother, tumors and cancers were intermingled. Even the specific method of tumor growth may be characteristic of a family. Thus in a family described by Hitchcock(1862) the tumors have the remarkable habit, throughout the family, of speeding up in middle age.

It seems probable that the precise nature of the symptoms shown in any case of neurofibromata is determined in large part, if not chiefly, by constitutional factors, and that in symptomatology of multiple neurofibromatosis, as in that of so many other diseases, we may distinguish biotypes—that is, family hereditary differences that are due to the specificity of the different germ plasms.

7. OTHER MULTIPLE TUMORS THAT ARE INHERITED IN THE SAME WAY AS NEUROFIBROMATA. There are many cases of formation of

multiple tumors that are perhaps related to multiple fibromatosis. Such, for example, is the group of telangiectases and polyadenomata.

(a) *Multiple Telangiectases.* This is a tendency to form vascular tumors in the skin and mucous membranes. These are sometimes hemispherical; at other times they have a "spider form;" in the latter type they are often associated with epistaxis. Examples are cited by Osler(1907), and numerous observers agree that the tendency recurs in successive generations, without skipping, and usually about half of the children of an affected parent are affected. This shows that the tendency to multiple telangiectasis is a dominant trait in heredity.

(b) *Polyadenomata of the Rectum.* Oidtmann(1917) has encountered 8 cases of polyadenomata of the rectum. Six of the patients belonged to two families, 3 sisters in one family, and mother, son and daughter in the other. References are given to nine other families showing from 2 to 6 cases, each of polyadenomatosis. A cancerous tendency is often present.

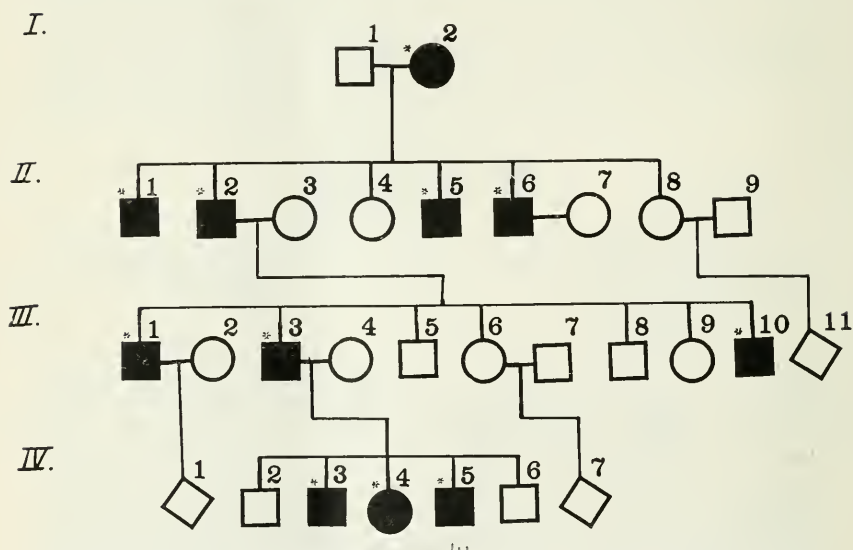


FIG. 35.—Pedigree chart of Blumer's (1892) family showing epidermolysis bullosa in four generations. Affected individuals are indicated by black symbols. The asterisk (*) indicates that the individuals were seen by Blumer.

Multiple fibromatosis, multiple telangiectasis and polyadenomata are the three classes of tumors (or tumor-like swellings) of which the inheritance has been carefully studied. It is remarkable that in all, inheritance seems to be of the simple dominant type, which we may interpret to mean that the tendency to form numerous "benign" tumors is due to some positive factor or to the presence of some unusual condition or substance that causes the rare reaction.

So, likewise, the tendency to form pigment patches in the skin—ephelides—is a dominant one, as Hammer has found.

Not only the tendency to form multiple tumors but numerous other skin troubles also are inherited as dominant traits. Examples of an inherited tendency to form bullæ or large edematous patches are: epidermolysis bullosa (Fig. 35), angioneurotic edema (Fig. 36) and persistent hereditary edema. Moreover, the diverse skin modifications seen in psoriasis, porokeratosis and ichthyosis have a positive hereditary basis, and ordinarily do not skip generations. Just what the usual dominance of all these abnormal skin conditions means (if it is anything other than chance) is quite obscure.

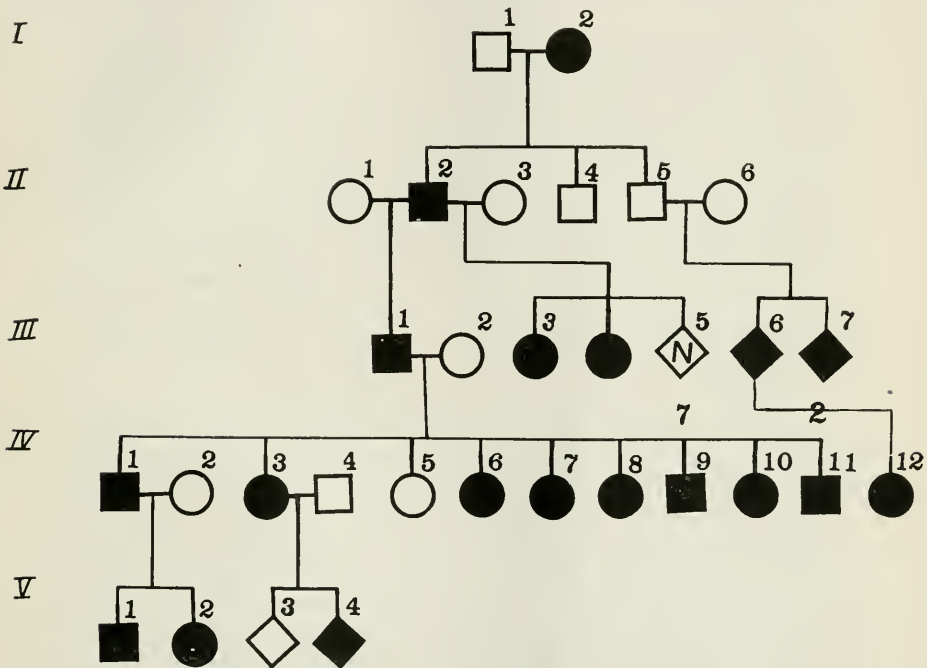


FIG. 36.—Pedigree chart of Osler's (1888) family, showing angioneurotic edema in five generations. Affected individuals are indicated by black symbols.

8. RELATION OF NERVE TUMORS TO CANCER. The tumors that we have been considering are mostly "benign." That is to say, they usually grow slowly and frequently cause no special inconvenience. If let alone they may remain as small as hazelnut-sized swellings until death intervenes at an advanced age. In some cases the tumor becomes larger and pendulous and the owner seeks to have it removed. Operations for this purpose have often been performed without recurrence of growth, at least for months, *e. g.*, Hitchcock (1862). On the other hand surgical interference is fre-

quently followed by regrowth, sometimes a sarcomatous growth of tissue at the point of removal of the tumor. As an example of the regrowth of a tumor we have Czerny's(1874) case, in which a part of a large tumor was removed, but the tumor continued to grow. In Hartmann's(1896) case a tumor on the crural nerve was removed but a new tumor quickly developed. As examples of sarcomatous growth we have Gilchrist's(1896) case, in which a removed tumor was replaced within five days by a sarcomatous growth, the mother of the patient having had tumors and a cancer. Also Barse's(1917) case, where, after removal of the tumor, the growth "then took on a very malignant course and recurred with startling rapidity; a microscopic examination of a portion of the tumor showed it to be a small spindle-celled sarcoma."

The nerve tumors are often of a sarcomatous nature. Thus in Adrian's(1901) case the largest tumor was a fibro-myo-sarcoma, while the other skin tumors showed the typical structure of neuro-fibromata. In Adrian's(1902) case, which showed multiple fibromata of the skin and viscera, the neurofibroma of the duodenum underwent sarcomatous degeneration. In Mathies's(1913) case there were tumors on the cranial and spinal nerves and "myxo-fibrosarcomata" of the peripheral nerves. Genersich(1870) also found, on microscopic examination, some of the tumors to be essentially fibromata, but some were distinctly sarcomatous and others myxomatous. Wedge-shaped masses in the lungs were sarcomatous.

9. BEARING OF FOREGOING FACTS ON HEREDITY OF CANCER. It is, of course, only in accord with common observation that tumors may develop into sarcomata or other malignant types of growth. The fact that multiple fibroneuromata do so bears on the question of "heredity of cancer," which is so much discussed.

This question is a perennial one. Of late it has come to the fore because of the doubt cast upon heredity of cancer by life insurance actuaries and statisticians using the method of mass statistics. On the other hand new evidence for the inheritance of cancer has come from the experimental pathologists who all agree that in mice there are strains that cannot grow cancers and others in which they grow rapidly. The hereditary behavior of such strains has even been investigated experimentally by Tyzzer and Little. Now the cancers of mice are so entirely like those of man that it is extremely probable that if the one has an hereditary basis the other has also.

Another reason for the view that cancer is hereditary is that there are races of men who are almost immune to cancers, such as the American Indian, full-blooded negroes and some aborigines of Australia and the Pacific Islands. Also, there are racial peculiarities in the organs affected by cancer; among the Japanese women cancer of the generative organs is about as common as in Great

Britain, but cancer of the breast only one-tenth as common. Also, we cannot overlook the significance of such facts as that of the occurrence of sarcoma of the eyeball in three generations in the direct line and four individuals of the middle generation of this family (Silcox 1892).

Finally, the fact of cancer villages, where there has been much intermarriage, is strong additional evidence of the racial significance of liability to cancer. In view of all these considerations we must consider the presence of an inheritable factor in cancer as practically certain. But we are, nevertheless, very far from a knowledge of the law of its inheritableness. That is a matter for future investigation.

10. **PATHOLOGY OF THE DISEASE.** There is a great deal of discussion regarding the pathology. It was in 1881 that von Recklinghausen(1882) called attention to the frequency of the association of multiple neuromas and cutaneous fibromas. He termed these latter neurofibromas, but later (1898), holding that the essential feature was an overgrowth of the connective-tissue envelope of the nerve bundles and of the endoneurium, and that the term neuroma should be restricted to tumors formed of proliferative nerve cells, he concluded that the tumors of this disease should be placed among the fibromata.

Knauss(1898) has described an instance in a girl, aged eleven years, of multiple subcutaneous growths of this order in which he discovered abundant ganglion cells.

The consensus of opinion seems to be that the tumor is neither a neuroma nor a glioma, but according to Adami(1911) a neurinoma or neurofibroma. "We deal with a condition of neuromatosis; the multiple nature of the growths along the continuity of the nerves demonstrates this. What is of interest in this connection is that in a large number of cases a study of the central nervous system showed the coincident existence of gliomatous areas in the brain and spinal cord. We deal with a tendency toward excessive vegetative activity of the nervous tissue, and where the condition affects the sympathetic ganglia there may develop true neuromas."

These tumors are to be differentiated from gummata, sarcomata, lepra and tuberculous nodules; but a careful inspection usually, and the microscopic examination always, will separate these conditions from the one under discussion.

The neurofibromata are slowly growing tumors of benign nature. Frequently they undergo a retrograde metamorphosis and show cystic, fatty or myxomatous degeneration. In some instances these tumors undergo sarcomatous transformation, assuming a malignant character, rarely then giving rise to metastases.

11. **DESCRIPTION OF THE NEW CASE.** CASE I.—M. G., aged forty-five years; male; born in Austria; peddler by occupation;

married; admitted to Montefiore Home and Hospital December 11, 1915; died September 29, 1916.

Family History. Father died at seventy-eight years, cause unknown. Mother alive and well. Negative for tuberculosis and cancer. No history of any degenerative disease in the family.

Personal History. Patient was always one of good habits, attended school, stating that he had never had any particular difficulties in his studies. Patient's first occupation was that of a painter, which he had to discontinue because he developed lead poisoning. He then became a peddler, continuing this occupation until a few months before admission to the hospital. He married at the age of twenty-five and his wife gave birth to eight children. The oldest has von Recklinghausen's disease and is mentally defective, and another child suffers from Hirschsprung's disease. (This child has since died.)

Past History. No diseases of childhood. No pneumonia, malaria, typhoid or rheumatism. Twelve years ago he was in Bellevue Hospital for two months, suffering from painter's colic. Eleven years ago he was operated upon in Bellevue Hospital for a tumor of the shoulder and neck, which had existed for one year.

Present Illness. This began twelve years ago. Soon after the attack of painter's colic he noticed the appearance of pigmented spots and of small tumor masses over the body. During this time he suffered from very frequent attacks of headaches, dizziness, palpitation and pain about the heart, at times associated with vomiting. The dizziness was frequently associated with staggering, so that, while walking, he was often falsely accused of drunkenness. Hearing of right ear impaired for six years. Vision of both eyes poor for the past five years. Attempts at reading a paper result in dizziness. No other organic disturbances. Has been in Mt. Sinai Hospital four times during the past eight years for the above complaints. The last time was two years ago.

For the past six months had headaches, with dizziness, pains about heart, with palpitation; pains all over body have become markedly aggravated. Of late he has also noted edema of lids and of the ankles, increasing during the day when up and about. During these six months has coughed a great deal, with mucoid expectoration, and has lost twenty-five pounds in weight.

Status on Admission. Patient is an adult male, poorly nourished, confined to bed and appears to be suffering from a chronic illness. Mental condition shows no evidence of inferiority or degeneration. The entire body, with the exception of the palms of the hands and the plantar surfaces of the feet, is covered with numerous pigmented areas varying in color from a light to a dark brown, confluent in the region of the neck. Nevi are present here and there and vary in size from a circular patch of one-sixteenth of an inch to an irregular-shaped nevus an inch or more in diameter. The

nodular elevations are in the main sessile, but a lobulated mass is present in the right temporal region (fibroma molluscum) and a pedunculated one in the region of the upper dorsal vertebrae. The masses vary in size from one-eighth of an inch to one inch. They are mostly soft, but a few hard ones are present here and there. The former are painful when squeezed between the fingers. The head is symmetrical and covered with an abundance of dry, dark brown hair.

Eyes. Conjunctivæ injected. Von Graefe's sign present. Pupils are equal, regular and react to light but poorly in accommodation. No nystagmus. Arcus senilis present in both eyes.

Ears and Mastoids. Externally negative. Hears watch with right ear at three inches, with left at fifteen inches.

Buccal Cavity. Mucous membranes of good color. Teeth in poor condition. No pyorrhœa. Tongue protrudes in median line; fine tremor present.

Neck. Symmetrical, rather long and thin. No abnormal pulsations visible. The cervical vertebrae are freely movable and there is good mobility of the entire vertebral column.

There is a very marked crepitation of the right shoulder on passive motion; less crepitation in the left. Patient complains of pain on moving the shoulder; no tenderness; no effusion in the joint. The muscles of the finger-joints are very hypotonic, especially those of the left hand. There are slight Heberden nodes in the small joints of the first, second, third and fourth fingers of the left hand and all the fingers of the right hand.

Both knee-joints crepitate. The ankle-joints appear normal. The joints of the toes also appear slightly hypotonic. No restriction of mobility of the knee-joints. The terminal phalanges of the fingers appear to be broader and shorter than usual. The epitrochlear glands are enlarged on the right side. Numerous rather small axillary lymph nodes. The inguinals are slightly increased.

Chest. Expansion poor, somewhat diminished on the right side. Respiration labored and accelerated. Supra- and infraclavicular retraction on both sides. Percussion note is hyperresonant and anteriorly except over a small area of precordial dullness. Over the whole chest expiration and inspiration are prolonged, expiration being of a higher pitch than inspiration. There are fine crepitant rales scattered over the whole chest, but they are more numerous over the right side. Posteriorly there is a hyperresonant note in both infrascapular regions. Respiratory murmur is emphysematous in character, with scattered fine rales from apex to base all over the chest.

Heart. Upper border is at the third space. Right border measured in the fourth space is at the right sternal border. Left border, in the fourth space, is 10 cm. from the median line. Apex

beat not visible or palpable; heard in the fifth space within the nipple line. Sounds are distant, regular, of good force; no murmurs. Radials are equal, regular, good force; vessels are thickened and slightly tortuous. Heart action is rather slow, 60 per minute. (This was not changed during the disease.)

Abdomen. Symmetrical; no signs of fluid; no distention. Liver, spleen and kidneys are not palpable. Slightly tender and very indefinite mass in the left hypochondrium.

Reflexes. Knee-jerks and Achilles and abdominal reflexes are exaggerated.

Sensation. Normal.

Fundi. Normal.

Blood-pressure. Systolic 115, diastolic 90.

Polygraphic tracings of the heart were normal.

Blood. Hemoglobin, 85 per cent.; red blood cells, 3,950,000; white blood cells, 13,800.

Differential White Blood Count. Neutrophiles, 84 per cent.; lymphocytes, 14 per cent.; large mononuclears, 1 per cent.; eosinophiles, 1 per cent. The eosinophile count, which in some cases of von Recklinghausen's disease, according to Galliard, runs as high as 15 per cent., was not raised in this patient.

Urine Examination. Light amber; acid in reaction. Specific gravity, 1010; albumin negative; sugar negative. Microscopic examination negative, except for a large amount of urates. Melanin negative.

Sputum Examination. Only once positive for tubercle bacilli.

Wassermann Reaction of Blood. Negative.

Roentgen-ray Examination. *Chest.* Marked infiltration of right upper lobe and inner portion of right lower lobes. Evidence of extensive adhesions at the median portions of the diaphragm on both sides. A number of dilated bronchi around both roots. Ascending aorta slightly dilated, showing abnormal pulsation.

Skull. Marked rarefaction of frontal bone. Faint outlines of anterior and posterior clinoid processes (softening). Sella turcica itself normal in size and shape.

Spine. Slight scoliosis of upper dorsal spine to left; of lower dorsal spine to right. No roentgen evidence of any other pathological change.

Hands. Bony excrescences at the bases of all the end phalanges. Moderate broadening of the basal portions of the middle phalanges of the second and fifth fingers. No arthritic changes in the bony parts of any of the joints.

Diagnosis. The diagnosis was obvious and was made on first examination. The patient was put on thyroid and suprarenin extract, with no effect. He was examined at short intervals and was noticeably becoming gradually weaker and weaker and the pigmentation more marked, especially around the neck, pectoral

region and abdomen. After some nine months' stay in the hospital he finally died of general asthenia.

Autopsy. The autopsy findings of the abdominal viscera proved negative, with the exception of the pigmentation in the liver and spleen. The examination of all the ductless glands as well as of the brain revealed nothing of note. There was evidence of chronic tuberculosis in the lungs.

Microscopic Sections. Microscopic sections were made by Dr. B. S. Klein, pathologist of the Montefiore Hospital, to whom we are indebted for the following description:

Skin. Section 1. In the subcutaneous tissue there is an area equal to several low-power fields, quite sharply marked off from the surrounding tissue. This area resembles nerve tissue throughout. In the lower layer of cells of the epidermis overlying there is a considerable amount of brown pigment. In the dermis a little below these latter cells there are a number of flat polygonal cells, with numerous brown granules in the cytoplasm. In a few places small extracellular clumps of brown granules are seen. In a few places in the subcutaneous nodule the elongated nuclei are less numerous than elsewhere, the cytoplasm of the cells is more prominent than elsewhere and has a more homogeneous structure. In the skin for some distance from the tumor the cells of the deeper layer of the epidermis and a number of cells in the dermis show a moderate to considerable amount of small brown granules. In another area of the section there is a nodule similar in appearance to the one described above, occupying an area less than a low-power field. Throughout the section the dermis is more dense in structure than normal; in many places the nuclei are fewer than normal; the tissue has a homogeneous uniformly pink-stained appearance, suggesting beginning hyalinization. Scattered throughout the nodule there are new-formed capillaries in fair abundance, most of them dilated. In the outer layers of the dermis, near the Malpighian layer, the tissue is quite structureless and in places has a stringy, bluish appearance. There are all stages between this appearance and that of the tissue suggesting nerve fibers, including a structureless, homogeneous pink-stained tissue. Scattered throughout the tumor are very many mononuclear eosinophilic cells not associated with other round cells and suggesting fixed tissue cells.

Section 2. Shows an area in the subcutaneous tissue larger than a low-power field fairly well circumscribed. The structure of this nodule is much denser than the one described above; in great part the tissue has a stringy blue-stained appearance and is homogeneous. Throughout this tumor and in the overlying dermis the bloodvessels are very tiny as compared with the vessels in corresponding areas in the tumor above described. In the dermis and epidermis overlying this tumor the pigmentation of the cells is much more intense. The latter tumor is apparently undergoing

degenerative change. There is also much homogeneous pink-stained tissue throughout.

Section 3. Shows throughout the section numerous brown granules in the cells of the deeper layers of the epidermis and of the scattered cells in the dermis. The portion of the dermis adjoining the epidermis is more dense in structure than normal. In places the tissue has a dense homogeneous pink-stained appearance, suggesting beginning hyalinization. Section of a nerve in the vicinity of these nodules shows at one place an accumulation of small mononuclear cells about a small vessel. The fibers show no apparent change.

Lungs. Section 1 shows the greater number of the alveoli and bronchioles filled with exudate. In the majority of places there are many polymorphonuclear leukocytes, a moderate number of mononuclear cells; some of these with engulfed blood pigment and débris, a varying number of red cells and a varying amount of serum. In places there is a fair amount of fibrin. The exudation is not uniform throughout; in places the spaces contain serum, a few desquamated cells and a few wandering cells. There are all gradations between alveoli of this character and those in which they are packed with polymorphonuclear leukocytes. The alveolar vessels throughout are moderately engorged. The exudate nowhere shows evidence of necrosis.

Section 2. Shows a number of large homogeneous structureless pink-stained areas, scattered throughout which there is considerable nuclear fragments and dust. Surrounding these areas there is a zone of epithelioid cells, and nearby these larger areas there are a few small (about one-sixth low-power field size) areas showing numerous epithelioid cells, scattered giant cells and peripheral nuclei, and about these a zone of small mononuclear cells. Also, in the neighborhood of these areas, the lung tissue is greatly scarred; there is considerable coal pigment and scattered small to fair-sized hemorrhages. A great many of the alveoli and bronchioles in the neighborhood are collapsed and in the walls there are seen several scattered typical proliferative miliary tubercles.

Section 3. Shows great scarring of the lung tissue and the scarred tissue has the appearance of hyalinization. There is considerable coal pigment scattered throughout. The alveoli and bronchioles are completely collapsed in great part. In places the scar formation is not so dense and here there are numerous prominent bloodvessels. In the section there is a portion of a large bronchus. At one place near the mucous glands there are seen three strips of true bone, composed of typical osteoblasts, surrounded by a homogeneous bluish-pink matrix, and surrounding these there is a thin layer of connective tissue. In the lumen of this bronchus there is a considerable amount of mucus, numerous polymorphonuclear leukocytes, a moderate number of mononuclear cells and

cell fragments. In places there is considerable desquamation of the epithelium. The connective tissue of the wall is increased in amount, in places very dense, homogenous, suggesting early hyalinization. In areas there are many dilated capillaries and scattered accumulations of round cells.

In all sections of the lung there are scattered areas in which the walls of groups of the alveoli are ruptured and good-sized spaces formed thereby. Some of these dilated spaces contain exudate similar to that described above.

Liver. Lobulation fairly distinct and fairly regular in the section. The cells all show evidence of postmortem change and are swollen and granular. They are slightly separated from each other. The cells in the central portion throughout contain much brown pigment. The capillaries contain many polymorphonuclear leukocytes.

Spleen. Shows a very slightly diffusely thickened capsule. The trabeculae are moderately increased in size and number; the Malpighian bodies are small, in places consisting of but a few cells about a bloodvessel and trabeculum. The nucleated cells in the pulp, however, are greatly increased in number. Scattered throughout the spleen there is a moderate amount of intra- and extracellular brown pigment. With the high power the sinuses seem to contain in places many polymorphonuclear leukocytes.

Pancreas. The tissue shows evidence of moderate postmortem change. The islands of Langerhans are fairly numerous and of good size. They show an apparent change, except that about a number of them there is an increase in the reticulum of the pancreas. The remainder of the parenchyma shows no other abnormality except that noted above.

Adrenal. There is some thickening of the capsule; the glomerular zone is not as prominent as normal; the tissue throughout shows evidence of moderate postmortem change. In the medulla there is a circumscribed area equal to a few low-power fields in which there are many large cells lying close to one another, suggesting ganglion cells. Some of these contain more than one nucleus.

Thyroid. The acini in general are of average size, lined by flat to cuboidal epithelium. Filled with amorphous deeply pink-stained material. The stroma is increased moderately in amount. In the regions of the increase the acini show slight to considerable atrophy. In one portion of the section there are three small circumscribed areas, one of them composed of acini much like those of the gland. The other two composed of smaller acini lined by cuboidal epithelium, more like the thyroid tissue of a child. About these areas there is a thick connective-tissue capsule.

CASE II.—THE SON. J. G., aged seventeen years; undersized for his age; an errand boy. Mentally he is distinctly below normal. Has been in a reformatory for three years.

He has adenoid facies and both upper lids droop, the right more than the left. In looking from the horizontal plane the middle of the upper lid crosses the iris of the pupils. Two median incisor teeth of the upper jaw missing, some of the lower in bad order. Numerous glands, supraclavicular, discrete, the size of an almond. The same is true in the axilla. Inguinals normal in size. Epitrochlears normal.

The whole complexion is dark. In addition there are numerous freckles all over the neck and trunk as far as the groin of both legs; these are dark brown in color, about 2 mm. in size. In addition there are about twenty larger areas of pigmentation; these are oval in shape, circular and vary in size from 1 to 5 cm. in diameter; they are darker in color and not elevated. There are few fibromata, one over the right clavicle, one on each forearm, one on the left upper arm and three on the back. There is one chalazion on the left upper lid and two on the lower lids. No hair in the axillæ and the areola of nipples are dark, 3 cm. in diameter. Eyes are prominent. There is a fibroma on the left supra-orbital ridge and on the left upper part of the chin.

Lungs. Negative.

Heart. Upper border, third rib; right border, right border of sternum; left border, 8 cm. from midsternal line. Apex beat not visible but palpable in the fifth space, 9 cm. from the median line. Heart action regular; normal in rate; no murmurs. Radials equal; regular; no increased tension; some thickening (pseudosclerosis).

Liver, Spleen, Kidneys and Abdomen. Negative.

Knee-jerks. Active.

Extremities. No edema.

Genitalia. Negative except for absence of pubic hair.

Has three brothers and four sisters who are said to be normal, excepting the one mentioned above, who has Hirschsprung's disease.

SUMMARY. 1. A description has been given of the occurrence of von Recklinghausen's disease in a father and son, with the autopsy findings in the case of the father, in whom the disease lasted thirteen years.

2. The presence of the disease in the son, associated with definite mental inferiority and delayed sexual development.

3. A review and analysis of the literature of 243 cases of multiple neurofibromatosis.

4. An analysis of 30 cases of the familial type, with charts of families in which there were two or more affected persons in one family. This establishes its hereditary tendency, showing the hereditary factor to be dominant, there being something in the germ plasm that positively facilitates the production, under appropriate stimulation, of tumors of the nerve sheaths.

5. The relation of neurofibromatosis to malignancy.

In conclusion, we wish to express our thanks to Dr. S. Wachsmann, medical director of Montefiore Home and Hospital, for permission to publish this case; to Dr. B. S. Oppenheimer, attending physician to Montefiore Home and Hospital, for many valuable suggestions in the preparation of this paper; and to Dr. B. S. Klein, pathologist to Montefiore Home and Hospital, for the preparation of the microscopic sections.

BIBLIOGRAPHY.

- Adami, J. George: Principles of Pathology, 2d edition, i, 758.
- Adrian, C. (1901): Ueber Neurofibromatose und ihre Komplikationen, Beitr. zur klin. Chir., xxxi, 1-98.
- Adrian, C. (1902): Ueber einen bemerkenswerthen Fall von Neurofibromatosis, Wiener klin. Wchschr., xv, 813-819.
- Albracht, K. (1906): Ein Fall von Rankenneurom am oberen Augenlid, Beitr. zur klin. Chir., Tübingen, L., pp. 614-620.
- Antelme, F. (1897): Un cas de molluscum fibreux elephantiasique, Review in Annales de Dermatologie et de Syphiligraphie, 3e série, ix (1898), 204-205. Original in Bulletin de la Société Médicale de l'île Maurice, October 29, 1897, p. 491.
- Arnozan, X. (1885): Névrome plexiforme, Jour. de Méd. de Bordeaux, xv, 72-73.
- Arnozan, X., et Prioleau, L. (1883): Sur les dermatofibromes congénitaux, généralisés, Annales de Dermat. et de Syph., 2 s., iv, 683-698.
- Atkinson, J. E. (1875): Observations upon Two Cases of Fibroma Molluscum, New York Med. Jour., xxii, 601-610.
- Audry (1901): Sur un cas de neurofibromatose avec scoliose, Société Française de Dermatologie et de Syphiligraphie, Bull. xii, pp. 143-144.
- Baldauf, L. K. (1915): Fibroma-Molluscum; Exhibition of Patient, Louisville Monthly Jour. Med. and Surg., xxii, 179.
- Barss, H. de B. (1917): A Report of Two Cases of von Recklinghausen's Disease (Neurofibromata), Jour. Michigan State Med. Soc., xvi, 113-116.
- Bassoe, P., and Nuzum, F. (1915): Report of a Case of Central and Peripheral Neurofibromatosis, Jour. Nerv. and Ment. Dis., xlii, 785-796.
- Berggrün, E. (1897): Ein Fall von allgemeiner Neurofibromatose bei einem 11 jährigen Knaben, Arch. f. Kinderheilkunde, xxi, 89-113.
- Billington (1914): Von Recklinghausen's Disease, British Med. Jour., 1914-1, p. 709.
- Blumer, C. (1892): Hereditäre Neigung zu Traumatisher Blasenbildung, (epidermolysis bullosa hereditaria), Arch. f. Dermatol. u. Syphilis, Ergänzungsheft, 1892, pp. 105-70.
- Bourey, P., et Laignel-Lavastine (1900): Un cas de maladie de Recklinghausen, Arch. gén. de méd., iv, 270-283.
- Bruns, P. (1870): Das Ranken-Neurom, Virchows Arch., l, 80-112, Nachtrag, pp. 108-112.
- Bruns, P. (1891): Ueber das Rankereneurom, Verhandl. der Deutschen ges. f. Clin., xx, Part II, pp. 151-159.
- Carwardine, T. (1899): Neuroma of Brachial Plexus, with Molluscum Fibrosum of Skin, Tr. Path. Soc., London, l, 27-29.
- Chiray et Coryllos (1905): Un cas de maladie de Recklinghausen.
- Clark, F. (1887): A Remarkable Case of Fibroma Molluscum, Lancet, 1887, i, 1183.
- Clark, S. N. (1917): Report of Cases of Folie à Deux. III, Med. Jour., xxxi, 395-401 (June, 1917).
- Cockayne, E. (1917): Case of Hereditary Neurofibromatosis (von Recklinghausen's Disease), Proc. Roy. Soc. Med., x, Section for Study of Disease in Children, pp. 33-34.
- Cole, H., and Shawan, H. (1911): Von Recklinghausen's Disease, with Report of Four Cases, Cleveland Med. Jour., x, 653-676.
- Collet, J., et Lacroix, E. (1893): Malformation congénitale de la face et du crâne, avec éléphantiasis des parties milles: nevromes plexiforme. Tumeurs multiple disseminées sur le tronc et les membres, Gaz. Hebd. de Méd. et de Chir., 1893, pp. 569-572.

Coupland, S. (1897): A Case of Multiple Subcutaneous Tumors (Probably Neuromata) Associated with Cranial Deformity (Frontal Osteoma), *Tr. Clin. Soc.*, London, xxx, 221-224.

Czerny, V. (1874): Eine Elephantiasis Arabum Congenita.

Darlos (1900): Dermatofibromes généralisés, *Annales de dermatologie et de syphiligraphie*, 4e serie, T. 1., 394-396.

De Haam, J. (1912): Ziekte van Recklinghausen. *Nederland Tijdsch. v. Geneesk.*, 1912, 1, 1492.

Deumié et Monéry, A. (1908): Un cas de maladie de Recklinghausen (neurofibromatose généralisée), *Arch. de méd. et phar. militaires*, Paris, lii, 177-184.

Feindel, E. (1896): Sur quatre cas de neurofibromatose generalisée, Thèse de Paris, 1896.

Fox, T., and Farquhar, T. (1876): On Certain Endemic Skin and Other Diseases of India and Hot Climates Generally, pp. 106-111.

Fraenkel, Joseph, and Hunt, J. Ramsay (1903): On Neurofibromatosis, *Med. Record*, June 13, 1903, lxiv, 925.

Galliard, J. (1906): Eosinophile sanguine dans la maladie de Recklinghausen, *Compt. rend. hebd. Soc. de biol.*, 1906, lxi, 563.

Genesich, A. (1870): Multiple Neurome, *Virchows Arch.*, xlix, 15-48.

Gilchrist, T. C. (1896): Two Cases (Including One in the Negro) of Molluscum Fibrosum, with the Pathology, *Johns Hopkins Hospital Reports*, i, 349-362.

Godet, G. (1906): Névrome Racémeux de la Paroi Thoracique, *Arch. Gén. de Méd.*, 1906, ii, 2327-2328.

Gordon, M. Holmes: *Osler's Modern Medicine*, 1st edition, vii, 503.

Gross, S. (1916): Epidermolysis bullosa hereditaria and "Erythromelie," *München. med. Wehnschr.*, lxiii, i, 323.

Guinon, L., et Reubsæet (1907): Un cas de maladie de Recklinghausen fruste, *Soc. de Pédiatrie de Paris*, ix, 263-267.

Harbitz, F. (1909): Multiple Neurofibromatosis (von Recklinghausen's Disease), *Arch. Int. Med.*, iii, 32-65.

Hartmann, H. (1896): Zur Kenntnis der sekundär malignen Neurome, *Beitr. zur klin. Chir.*, Tübingen, xvii, 177-184.

Hashimoto, T. (1890): Fibroma molluseum, *Ztschr. f. klin. Med.*, xvii, 352-360.

Hecker, C. (1858): Die Elephantiasis oder Lepra Arabica, *Lahr.*

Herzfel, E. (1890): Ueber Fibrome und Sarkome bei peripheren Nerven, *Beitr. zur path. anat. und zur allg. path.*, viii, 38-70.

Herxheimer, G., and Roth, W. (1914): Zum Studium der Recklinghausenschen Neurofibromatose, *Beitr. z. path. anatomie und z. allgen. pathol.*, lviii, 319-389.

Hesselbach, C. M. (1824): Beschreibung der Pathologischen Präparate zu Würzburg, Giessen, 1824, p. 284.

Hintz, A. (1909): Zur Kenntniss der Morbus Recklinghausen, *Wien. klin. Wehnschr.*, xxii, ii, 1156-1158.

Hirsch, E. (1911): Zur Kasuistik des Morbus Recklinghausen im Kindesalter, *Prager med. Wehnschr.*, xxxvi, 375-376.

Hirst, B. (1911): A Note on the Etiological Influence of Pregnancy upon Molluscum Fibrosum, *Am. Jour. Obst.*, lxiii, 256-257.

Hitchcock, A. (1862): Some Remarks on Neuroma, with a Brief Account of Three Cases of Anomalous Cutaneous Tumors in One Family, *AM. JOUR. MED. SC.*, xliii, 320-328.

Iniguez, F. (1880): *Molusco pendulo generalizzato*, *Tr. by Soresina from the Revista Especial de Oftalmologia Sifiligrafia, Dermatologia y Affecionas Urinarias di Madrid*, March 15, 1880, and printed in *Giornale Italiano delle Malattie Veneree e della Pelle*, 1880, p. 171.

Johnson, H. (1906): Two Cases of von Recklinghausen's Disease, *Jour. Roy. Army Med. Corps*, vi, 696-699.

Karplus, J. (1915): Hereditärer Syringomyelie. *Klintherapeutische, Wehnschr.*, xxii, 1915, ii, 539.

Keyser, C. (1905): A Case of von Recklinghausen's Disease, *Tr. Clin. Soc.*, London, xxxviii, 208-09.

Klippel, M., et Maillard, G. (1906): Un cas de Recklinghausen avec dystrophies multiples et predominance unilatérale, *Nouvelle iconographie de la Sâlpêtrière*, xix, 282, 288.

Knauss, K. (1898): Neuroma verum multiplex amyelinicum gangliosium, *Arch. f. path. Anat. (etc.)*, Berlin, 1898, cliii, 29-59.

Kolepke, E. (1911): Ueber zwei Falle von Multipler Neurofibromatose (Recklinghausenscher Krankheit) mit Verkrümmung der Wirbelsäule, *Ztschr. f. orthopäd. Chirurg.*, xxix, 367-393.

Kolpin, O.: Ein Fall von Fibroma Molluscum Multiplex, Inaug. Diss., Greifswald. Königsdorf, C. (1889): Ein Fall von Fibroma Molluscum Multiplex, Inaug. Diss., Würzburg.

Labouverie, J. (1899): Considerations à propos de quelques cas de neurofibromatose generalisee, Thèse de Nancy, 1899.

Laignel-Lavastine, et Leroy, R.: Case Presented by Bourcy, 1905, Nouveau cas de Neurofibromatose avec autopsie: présentation de nerfs, *Soc. Méd. des Hôp. de Paris*, xxii, sér. 3, 122-125.

Lambert, O., et Girard (1908): Neurofibromatose généralisée, Énorme tumeur royale, *L'Écho Médical du Nord*, xii, 30-33.

Lange, E. (1906): Die Rolle der Heredität in der Aetiologie der Neurefibrome, *Fibromata mollusea, Elephantiasis congenita*, Inaugural Diss., Leipzig, 1906.

Langmead, F. (1910): A Case of Hereditary Multiple Telangiectases, *Proc. Roy. Soc. Med.*, iii, Pt. I, Clin. Sect., p. 109.

Leclerc, M. (1908): Maladie de Recklinghausen et paralysie rediculaire du plexus brachial, *Lyon Médical*, iii, 1092-1098.

Leriche, R. (1911): Ueber einen durch Neurofibromatose bedingten Fall von Pylorusstenose, *Deutsch. Ztschr. f. Chirurg.*, iii, 314-320.

Lion, G., et Gasne, G. (1904): Maladie de Recklinghausen, *Soc. Méd. des Hôp. de Paris*, 3e, série, xxi, 5-18.

Littlewood, H., Maxwell, W. H., Telling and Scott (1905): A Case of Multiple Neurofibromatosis, *Lancet*, 1905, ii, 921-923.

Malherbe, H. (1901): Neurofibromatose généralisée lésion des glandes sudoripares, *Jour. des maladies cutanées et syphilitiques*, xiii, 613-621.

Marie, P. (1903): Quoted by Fraenkel and Hunt (1903) q. v.

Marie, P., et Bernard, A. (1896): La neurofibromatose generalisee, *Gaz. des Hôp.*, 69e, Année, pp. 303-304.

Marie, P., et Convalaire: Quoted by Oppenheim, *Text-book of Nervous Diseases*.

Mathies, A. (1913): Vier familiäre Fälle multipler Neurofibrosarkomatose, *Ztschr. f. klin. Med.*, lxxvii, 50-66.

Meek, E. (1905): A Case of Neurofibroma (Disease of Recklinghausen), *Boston Med. and Surg. Jour.*, clii, 370-372.

Menke, W. (1898): Rankenneuron mit allgemeiner Multiplicität von Neuomen, *Berl. klin. Wehnschr.*, xxxv, 974-976.

Moses (1890): Fibromes multiples mous héréditaires avec éléphantiasis mou, *Semaine médicale*, x, 450-451.

Mosse (1907-8): Thèse de Lyon, No. 15.

Moutier, F. (1906): Maladie de Recklinghausen avec Nevrome plexiforme du dos de la main, *Rev. Neurologique*, xiv, 1081-1082.

Moynihah, B. (1901): A Case of Generalized Neurofibromatosis with "False Neuroma" of the Vagus Nerve, *Lancet*, 1901, i, 28-29.

Murray, J. (1873): On Three Cases of a Peculiar Form of Molluscum in Children, *Lancet*, 1873, i, 410-411.

Naegeli, O. (1916): Naevi anaemici und Recklinghausensche Krankheit, *Arch. f. Dermat. und Syph.*, cxxi, 742-745.

Neumann (1897): Fibrosom molluscum, *Arch. f. Dermat. und Syph.*, xxxix, 117.

Oeterlony, J. (1875): A Case of Molluscum Simplex, with Illustrations, *Arch. Dermat.*, i, 300-304.

Oidtmann, A. (1917): Familial Polyadenomatosis in the Rectum, *Nederlandsch. Tijdschrift voor Geneeskunde, Soc. Proc.*, 1917, i, 2184.

Oppenheim, H.: *Text-book of Nervous Diseases*, Edinburgh, 5th edition, i, 601.

Osler, W. (1888): Hereditary Angioneurotic Edema, *AM. JOUR. MED. SC.*, xcv, 362-67.

Oulmont et Haller (1909): Un cas de neurofibromatose généralisée, *Bull. et Mém. Soc. Méd. des Hôp. de Paris*, xxvii, 3e. sér., pp. 707-715.

Parsons, P. (1906): A Case of Recklinghausen's Disease, *Med. Press and Circular*, London, lxxxi, 68-69.

Pic and Gauthier (1908): *Lyon Méd.*, 1908, exi, 1148.

Pic and Rebattu (1908): *Lyon Méd.*, 1908, cviii, 636.

Pick, F.: Ueber das Molluscum, *Wien. med. Wehnschr.*, 1865, pp. 901-905.

Piollet, P. (1902): Neurofibromatose généralisée avec énorme tumeur royale, du poids de 5k, 600 et 602 tumeurs satellites beaucoup plus petites, *Gaz. des Hôp.*, 75e Année, pp. 1345-1350.

Poncet (1909): *Bull. et mém. Soc. Méd. des Hôp. de Paris*, 1909, 3e sér., xxvii, p. 714.

Rapok, O. (1890): Beiträge zur Statistik der Geschwülste, *Deutsch. Ztschr. f. Chir.*, xxx, 465-543.

Recklinghausen, F., von (1882): Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen, Berlin.

Rolleston, H. (1899): A Case of von Recklinghausen's Disease Complicated with a Sarcomatous Growth Involving the Brachial Plexus, *Lancet*, 1899, ii, 271-273.

Rolleston, J., and MacNaughten (1912): Familial von Recklinghausen's Disease, *Rev. Neurol. and Psychiat.*, x, 1-10.

Rolleston, J. (1917): Hereditary and Familial von Recklinghausen's Disease, *Proc. Roy. Soc. Med., Section for the Study of Disease in Children*, x, 32-33.

Roubinovitch, J., et Regnault de la Soudière (1914): Deux cas de Neurofibromatose familiale dont un avec pseudo-chéiromégalie unilatérales, *Rev. neurol.*, xxviii, 110-111.

Rüdler, F. (1904): Un cas de neurofibromatose généralisée, *Nouvelle Iconographie de la Sâlpêtrière*, xvii, 203-206.

Salomon, G. (1878): Multiple Neurome bei einem schwachsinnigen Individuum. Fortschreiten der Neurom-bildung während der Dauer der Beobachtung. Exstirpation und mikroskopische Untersuchung eines Neuroms, *Charite-Annalen*, iv (1877), printed 1879, 133-143.

Schiffner (1818 and 1822): *Med. Jahrb. des Oestreich. Staats*, Bd. iv, St. 4, p. 77, and Bd. vi, St. 4, p. 44.

Sequeira, J. (1916): Sebaceous Adenoma (Pringle Type) in Mother and Daughter, *Proc. Roy. Soc. Med.*, x, Section of Dermatology, p. 15.

Smith, Robert William (1849): A Treatise on Neuroma, Dublin, Hodges & Smith.
Speransky, N. (1895): A Case of Multiple Fibromata of the Skin, *Dermatol. Ztschr.*, ii, 399-401, Verhandlung der Dermatologischen und Venerologischen Gesellschaft zu Moskau, Sitzung vom 21 Januar, 1895.

Spillmann, P., et Etienne, G. (1898): Six cas de neurofibromatose (neurofibromatose medullaire et peripherique), *Gaz. hebdom. de Méd. et de Chir.*, nouvelle serie, iii, 673.

Strümpell, Adolph (1911): A Text-book of Medicine, 4th Am. edition, ii, 278.

Sutherland, A. (1906): Case of (?) von Recklinghausen's Disease, *Clin. Soc. Trans.*, xxxix, 245-246.

Tailhefer, E. (1897): Fibromes multiples et congénitaux de la peau, *Le Progrès Médical*, 1897, pp. 474-475.

Thomson, A. (1900): On Neuroma and Neurofibromatosis, Edinburgh, Turnbull & Spears, 168 pp.

Tichoff and Timofejeff (1894): Multiple Neurome mit Fibroma molluscum multiplex, *Chir. Annalen, russ.*, 1894, p. 719.

Trimble, W. (1911): Remarks on Neurofibromatosis, *New York Med. Jour.*, xciii, 358-360.

Vignolo-Lutati, C. (1911): Beiträge zur Recklinghausenschen Krankheit. Klinische, pathologisch-anatomische und histologische Beobachtungen, mit besonderer Berücksichtigung des Hautnervensystems, *Monats. f. prak. Dermatol.*, lii, 51-70.

Vignolo-Lutati, C. (1916): Neurofibromatosis with Addison's Syndrome, *La Riforma Medica*, xxxii, ii, 1061-1064.

Virchow, R. (1847): Ueber die Reform der Pathologischen und Therapeutischen Anschauungen durch die mikroskopischen Untersuchungen, *Virchows Arch. f. path. Anat. und Phys. u. f. klin. Med.*, i, 207, lv, 226.

Walsh, D. (1908): Case of Fibromata of the Skin, with Developing Neurofibroma, *Proc. Roy. Soc. Med.*, i, pt. 1, Dermatological Section, 189-190.

Weber, F. (1909): Cutaneous Pigmentation as an Incomplete Form of Recklinghausen's Disease, with Remarks on the Classification of Incomplete and Anomalous Forms of Recklinghausen's Disease, *British Jour. of Dermatol.* xxi, 49-53.

Wolfsohn, G., and Marcus, E. (1912): Neurofibromatosis und Akromegalie, *Berl. klin. Wehnschr.*, xlix, i, 1088-1090.

Zentmayer, William (1912): A Case of Plexiform Neurofibroma Involving the Orbit, *Tr. Am. Ophthal. Soc.*, xiii, 4 pp. 1 pl.

THE TEETH AND TONSILS AS CAUSATIVE FACTORS IN ARTHRITIS.

By ROLAND HAMMOND, M.D.,

PROVIDENCE, R. I.

FROM the earliest days of medical science the teeth and tonsils have been considered as having a causal relationship to arthritis. This is shown by the use of the terms "rheumatic tonsils" and "gouty gums." These conditions were formerly supposed to be induced by exposure to cold or to an excess of uric acid or lactic acid in the blood, or to some unknown disturbance of the metabolism.

Of late years the infectious theory of arthritis has been steadily gaining ground. This theory results from the discovery of microorganisms in or around the joints and also because arthritis has been observed frequently to follow various local and general infections.

The conception that a general systemic disease, such as arthritis, could arise from a local infection was appreciated early in the development of medical science. Until recent years, however, the apparent connection was recognized only when a condition of surgical sepsis preceded the arthritis.

The newer concept of the subject, to which the term focal infection has been applied, presupposes a circumscribed area of tissue infected with microorganisms. This area of infected tissue, the primary focus, is generally obscure in nature, often difficult to locate, and usually has no apparent connection with the secondary focus located in the articular structures. The broader interest in this subject has been brought about by a better knowledge of bacteriology, of modes of infection and by coöperative laboratory and clinical research.

Chronic infection of the tonsils and lymphoid tissue of the nasopharynx is exceedingly common in childhood, while acute rheumatic fever is relatively rare at that age. On the other hand the onset of rheumatic fever following an infection of the mouth and throat is too well recognized to be controverted.

Alveolar abscess is so prevalent as to be regarded as well-nigh universal, and yet it is not commonly associated with systemic infection. The protective forces surrounding the abscess are so efficient in the great majority of instances, and the lesion becomes so thoroughly walled off, that many thoughtful physicians and dentists deny the possibility of this condition becoming a focus of infection except on rare occasions.¹

¹ Billings, Frank: Focal Infection, New York, 1916, 6.

In certain cases, however, the etiological relation of localized infection to both acute and chronic systemic disease seems too evident to be set aside. Numerous cases reported by various workers testify to the marked improvement observed when a localized area of infection has been removed.

The bacteria most commonly found in areas of local infection are the members of the streptococcus group. Their usual habitats are the regions of the teeth, the tonsils and the nasal accessory sinuses. Careful questioning will often elicit symptoms pointing to existing infection in these structures or in some other part of the body.

A coöperative study of the patient should be made, including examinations by dentists, by ear, nose and throat surgeons, and when necessary by other specialists. A careful roentgen-ray study of the teeth and accessory sinuses is always advisable and frequently absolutely indispensable.

Laboratory examinations of pathological material should always be made. Cultures should be taken from the depths of tonsillar pockets and alveolar abscesses and not from the surface of the gums or tonsils.

In addition, it is necessary to examine fluid aspirated from joints or small bits of synovial membrane or lymph glands, or muscle tissue may be removed for pathological study. A Wassermann test should always be made to eliminate a syphilitic joint involvement.

The work of Rosenow² has shown what is apparently a remarkable transmutability of the members of the streptococcus group. A strain of the *Streptococcus viridans* isolated from the blood of a case of chronic infectious endocarditis was cultivated in various media, and animals were inoculated with successive strains. The end-result was a pneumococcus. The bacteria were typical pneumococci and transmutation of the original pure culture of *Streptococcus viridans* had occurred in form, cultural characteristics and in general and special pathogenic virulence for animals. Rosenow has also observed that the property of transmutation is reversible within the members of this family.

Many eminent bacteriologists in this country have been unable to duplicate Rosenow's³ experiments in bringing about transmutation of the members of the streptococcus group, and his conclusions are not accepted by many equally prominent laboratory workers.

The results of Rosenow's experiments show that the streptococci often have a remarkable affinity or tropism for the organs or tissues from which they were isolated.

At autopsy oftentimes no other focal lesions could be found

² Transmutations within the *Streptococcus Pneumococcus* Group, *Jour. Infect. Dis.*, 1914, xiv, 1.

³ Elective Localization of Streptococci, *Jour. Am. Med. Assn.*, 1915, lxx, 1687.

except those in the organ in question. The cells of the tissues for which a given strain shows elective affinity take the bacteria out of the blood stream as if by a magnet.

Individual animals, like human beings, are found to vary in their ability to resist infection. Certain virulent bacteria seem to have the property of rendering the tissues less favorable for their growth. On the other hand the less virulent bacteria tend to make this soil more favorable. Some property evidently exists in the tissues of the individual harboring a focus of infection which permit the bacteria to develop changes in virulence under varying degrees of oxygen pressure and in mixed culture. The susceptibility of the host is far more important than the specificity of the infecting microorganism.

DISEASED CONDITIONS OF THE TEETH AND ARTHRITIS. Over a century ago Benjamin Rush⁴ reported the cure of a case of rheumatism in the hip-joint by extracting a tooth. Referring to decayed teeth he says: "I am disposed to believe that they are often the unsuspected causes of general and particularly of nervous diseases. . . . Our success in the treatment of all chronic diseases would be very much promoted by directing our inquiries into the state of the teeth in sick people and by advising their extraction in every case in which they are decayed. It is not necessary that they should be attended with pain in order to produce diseases." In the light of modern scientific work the above statement is almost prophetic.

Apparently no further attention was paid to this subject until the latter part of the nineteenth century, when we find Ingersoll,⁵ Witzel⁶ and Reese⁷ advocating the removal of all decayed teeth which are not absolutely necessary for good articulation. In 1899 William Hunter⁸ called attention to diseased conditions in the teeth, gums and alveolar processes and suggested the term "oral sepsis" or medical sepsis. He believed it to be of much more common occurrence than surgical sepsis. His article included a scathing denunciation of American mechanical dentistry, with special reference to crown- and bridge-work and the stomatitis existing under artificial plates. With our present knowledge this criticism was more or less justified.

Shortly afterward Price⁹ referred to root canals as the "dentists' graveyard, where so many cover up careless and defective work, trusting it will never come to light."

⁴ Medical Inquiries and Observations, Philadelphia, 1819, i, 1917.

⁵ Sanguinary Calculus, Ohio State Jour. Dent. Sc., 1899, i, 189.

⁶ The Treatment of Pyorrhœa Alveolaris or Infectious Alveolitis, British Jour. Dent. Sc., 1882, xxv, 153.

⁷ Uremia and its Effects upon the Teeth, Dental Cosmos, 1886, xxviii, 550.

⁸ Dental Diseases in Relation to General Diseases, Especially to Infective Gastritis, Odont. Soc. Tr., 1898-99, xxi, 92.

⁹ Practical Progress in Dental Skiagraphy, Items of Interest, 1901, xxiii, 458.

Broomell¹⁰ called attention to the deleterious effects of inserting large gold fillings near living tooth pulps and likewise the placing of gold-shell crowns without removing the pulp. Chayes¹¹ has characterized mechanical bridge-work as unsatisfactory, incomplete, unwholesome and unclean.

Kenneth Goadby¹² was the first to point out the direct relationship of dental infections to joint infections. By the removal of infected teeth he was able to produce a cure in 3 cases, one of which had been completely disabled for many months. From these patients he isolated an organism which he called the *Streptobacillus malæ*. This organism by animal inoculation produced joint disease in rabbits.

Hartzell and Henrici¹³ have for several years conducted a systematic research, including animal inoculation, into the relationship of mouth infection to metastatic infection of other parts of the body. Patients presenting joint infection were referred to them for investigation and treatment of mouth conditions. A complete roentgenographic examination of the teeth and jaws was first made. Whenever dental abscesses were present the abscessed teeth were isolated with dry gauze, the tooth or root was cleansed with iodine and wherever possible the tissue about the neck of the tooth was cauterized. The tooth was extracted and the root tip amputated with sterile forceps and immediately dropped into culture media. The resulting growth has invariably produced, among other bacteria, the *Streptococcus viridans*. This organism was found in the confined dental abscess, in the superficial tissues of the peridental membrane and even in the roots of healthy living teeth. These writers believe that the dental path is commonly infected with this organism.

SUSCEPTIBILITY OF THE TOOTH TO INFECTION. Certain anatomical conditions resulting from the development of the teeth render them particularly susceptible to infection from without. The union of the mucous membrane to the tooth structure is always imperfect and capable of admitting infection. The dental structure has no protecting device save its coat of enamel. If this be in any way imperfect there are no antibodies or protecting leukocytes in the saliva to save it from the disintegrating effect of bacterial action.

The structures about the tooth are not well adapted to resist infection from the tooth. The gingival crevice, or gum marginal crevice, is protected externally by tough pavement epithelium, but has almost no epithelial protection at its point of union with the tooth itself. Through destruction of enamel, dentin and from

¹⁰ The Adventitious Effects of Large Masses of Gold in Contact with Tooth Tissues, *Dental Cosmos*, 1910, lii, 389.

¹¹ Empiricism of Bridge-work, *Items of Interest*, 1910, xxxii, 745.

¹² The Relation of Diseases of the Mouth to Rheumatism, *Practitioner*, 1912, lxxxviii, 107.

¹³ The Dental Path: its Importance as an Avenue to Infection, *Surg., Gynec. and Obst.*, 1916, xxii, 18.

suppurating pulps the teeth present 32 separate sources of infection. There are also 32 open dental alveoli and 30 spaces between the teeth which are susceptible to infection. The generous blood supply at this point allows microorganisms to pass readily into the openings in the bottom of this crevice and so into the deeper tissues by way of the lymph and blood streams.

Microorganisms have been found in freshly opened pulp chambers where no evidence of disease existed. A putrescent mass in the pulp chamber may exist for months or years because the walls cannot collapse and are incapable of bringing about the natural cure of an abscess as is possible in other parts of the body.

PYORRHEA ALVEOLARIS. This disease has been recognized for several centuries, but was first described by Riggs in 1867. It is strictly a disease of the peridental membrane and is indicated by a progressive destruction of the root membrane of the tooth commencing at the gingival border, generally accompanied by a flow of pus and destruction of the alveolar walls. Pus is absorbed into the blood and lymph channels, into the tissues adjacent to the teeth and from the gastro-intestinal tract by swallowing. A few years ago a considerable furor was created in the profession by the discovery of the *Endameba buccalis* in the pyorrhœal pockets of those suffering from the disease. This protozoa had been long known, but Barrett¹⁴ was the first to consider it as an etiological factor in pyorrhœa alveolaris. Bass and Johns¹⁵ believe it to be the cause of this disease.

On the other hand, Sanford and New¹⁶ hold that before *Endameba buccalis* can be regarded as the cause of pyorrhœa alveolaris its pathogenicity must be demonstrated by animal experimentation. They also believe that before the alkaloids of ipecac can be accepted as the cure of this disease it must be established that they actually destroy the amebæ in the mouth.

Billings¹⁷ believes that the endamebæ play an important part and permit infection with the pyogenic bacteria. The bacteria are the important factors in causing the general infection.

ROENTGENOGRAPHY IN DENTAL CONDITIONS. The roentgen rays are of the greatest value in accurately diagnosing certain diseased conditions of the teeth which are considered to have an etiological relation to arthritis. Probably its greatest field of usefulness is in locating abscesses around the apices of non-vital teeth. Such infections may occur without pain and without clinical evidence of their presence. If their location is such that they can discharge

¹⁴ The Protozoa of the Mouth in Relation to Pyorrhœa Alveolaris, Dental Cosmos, 1914, lvi, 948.

¹⁵ Pyorrhœa Dentalis and Alveolaris; Specific Cause and Treatment, Jour. Am. Med. Assn., 1915, lxiv, 553.

¹⁶ The Relation of Amebiasis to Pyorrhœa Alveolaris, Surg., Gynec. and Obst., 1916, xxii, 27.

¹⁷ Focal Infection, New York, 1916, 6.

their contents into the system—for example, by way of the antrum—their presence may remain unsuspected until diagnosed by the roentgen rays. In other teeth the abscess may protrude as the familiar gum-boil, which ruptures and may finally establish a fistula.

It must be clearly stated at the outset that an abscess may exist which cannot be revealed by the roentgen rays. This is because the pus is thinly distributed in a certain area or because the bone has not been sufficiently robbed of its lime salts to make this loss clear on the roentgenogram. The first appearance is a small area of slight bone rarefaction around the root apex. This process may go on to destruction of bone with cavity formation, resulting in the blind dental abscess or a fistulous connection with the mouth may be established. These blind abscesses often heal spontaneously. Under such favorable conditions the laying down of lime salts and the subsequent regeneration of bone can be followed with precision in roentgenograms made at intervals.

The interpretation of dental roentgenograms is full of pitfalls. Unless one is familiar with dental anatomy and pathology, and the varying appearance of shadows produced by roentgenograms taken from different angles, serious errors will be made. It is possible to take a roentgenogram from such an angle that an apical abscess is apparently demonstrated. A plate or film made from a slightly different angle will disclose only the normal bone surrounding the tooth apex. The reason for this error lies in the fact that at certain angles the shadows of the nasal cavity or antrum may overlie the tooth root and simulate the appearance of an abscess.

The point is that an apical shadow merely signifies decalcification of bone from any cause. It may represent a slow change, such as atrophy or absorption from long-continued irritation or pressure; it may mean an acute infective process or it may signify the remains of former disease—scar tissue. These shadows do not necessarily indicate the presence or absence of pus. This fact can be determined only by a study and correlation of the symptoms and clinical findings.

Other conditions which may cause symptoms referable to the teeth, and which can be differentiated by the roentgen rays, are calcareous concretions or stones in the pulp of the teeth, cysts of the jaw, dentigerous cysts and unerupted or impacted teeth.

RELATION OF DENTAL INFECTION TO SYSTEMIC CONDITIONS. In many cases there is a tendency to overestimate the role of these infections in causing more serious diseases. It is difficult to establish the etiology, as, for example, in a case of chronic arthritis of several years' standing. Dental examination shows several non-vital teeth. The roentgenogram may reveal any degree of change from a slight rarefaction of bone to a blind abscess. The teeth have been filled for many years and have given no trouble. The joint infection is hematogenous and a certain percentage of periapical

infections are hematogenous. Why may not both of these infections have resulted from a mild general bacteriemia and have developed coincidentally? Also, if the joint condition came first, why may it not have caused the dental condition? Other infections are quite as likely the cause as those in the mouth. Arthritic cases by no means always clear up after mouth infection has been removed. Many innocent teeth are being sacrificed from insufficient data, such as a crudely interpreted roentgenogram. Worse than this, several fatalities from ill-advised extraction of teeth during periods of exacerbation have been reported. It is well to remember the remarkable ability of the tooth and adjacent structures to bring about the spontaneous cure of a blind dental abscess with no resulting systemic involvement. Were this not so the human race would long since have been exterminated.

DISEASED TONSILS AND ARTHRITIS. The close connection between tonsillitis and arthritis has been recognized for at least a century and probably much longer. At times the joint and throat symptoms are simultaneous in their onset; at other times the tonsillitis precedes the arthritis and may even completely subside before the joint lesions develop. Subacute and chronic infectious arthritis are often associated with recurring attacks of tonsillitis, the tonsils lighting up previous to each fresh exacerbation of the joint lesions. On the other hand the tonsils may be the seat of a low-grade chronic inflammation lasting for months, with frequent outbreaks of a more acute character.

The pathological conditions to which the tonsils are subject are generally attributed to the peculiar anatomical structure of the crypts and their tendency to retain cellular débris. The crypts are tortuous and deep, extending nearly to the capsule; their walls are held in close apposition by pressure of the surrounding lymphoid tissue. The mouths of the crypts may be partially closed by the plica triangularis or the upper wall of the supratonsillar fossa, and, in addition, the supratonsillar crypts drain upward. The result is that a certain amount of débris is found in the crypts of all tonsils. Bacteria enter the crypts and develop under ideal conditions for growth. The cryptic epithelium is usually composed of only one or two layers of cells and offers little mechanical resistance to the entrance of foreign material. The conditions are thus seen to be ideal for the invasion of bacteria and the absorption of the toxic products of their growth.

Disease in the middle ear, the accessory sinuses, conjunctivæ, teeth and alveolar processes may be the cause of chronic disease of the tonsils. On the other hand, obstruction of the upper air passages by hypertrophy of the tonsils and adenoid overgrowth prevents proper drainage from the nasal cavities and accessory sinuses and leads to infection of the middle ear, the sinuses of the head and the mucous membrane covering the turbinate bodies.

In subacute and chronic arthritis the deep crypts almost invariably show pure cultures of the *Streptococcus hemolyticus*, which produce acute or chronic multiple arthritis when injected into animals.

The presence of these organisms in the tonsillar crypts of patients with joint lesions and the experimental results in animals suggest a causal relationship of the tonsils to arthritis.

OPERATIONS ON THE TONSILS. The advocates of partial removal have been influenced by the possible loss of some unknown function which would be detrimental to the patient and have counselled against complete removal of the tonsils. Those who believe in the operation of complete tonsillectomy point out the fact that thousands of these operations have been performed of late years, with no untoward result which could be attributed to the loss of any possible functioning power. It is also said that the histological structure of the tonsils shows that their function, whatever it may be, is identical with that of other lymphoid nodules of the body. This function, they claim, would no more be missed than the removal of a small piece of skin.

In the absence of any definite theory as to their function it seems reasonable to believe that they have a purpose even if it has not so far been discovered. They should never be removed, especially in children, without adequate cause. Before advising ablation the physician should be convinced that the tonsil is so completely diseased that it cannot functionate properly. Many tonsils are capable of overcoming infection in certain of their crypts. As a result a healed process may be present which, to the inexperienced, would denote active disease.

Wright¹⁸ and others assert that the tonsils enlarge regularly during the periods of dentition, the enlargements occurring about the second, sixth, twelfth and seventeenth years. These enlarged tonsils, if not infected, return to normal when the teeth have completely erupted. This is a most potent argument against their removal at these periods, when the hypertrophy is evidently a response to some physiological stimulus.

Crowe, Watkins and Rothholz¹⁹ believe that partial occlusion of the crypts from partial tonsillectomy renders the patient more liable to secondary cardiac, joint and renal lesions. They have observed 8 cases with frequent attacks of tonsillitis for many years preceding, but never with anything but local symptoms. With the idea of stopping these attacks each of these patients had had a partial tonsillectomy performed with the guillotine or with the electric cautery under local anesthesia in each case. All went well

¹⁸ A Functional Relation of the Tonsil to the Teeth, Boston Med. and Surg. Jour., 1909, cx, 635.

¹⁹ Relation of Tonsillar and Nasopharyngeal Infections to General Systemic Disorders, Bull. Johns Hopkins Hosp., 1917, xxviii 1.

until the next coryza, when joint symptoms appeared for the first time. Portions of the tonsils showed the crypts obscured by scar tissue. After their removal the joint symptoms gradually disappeared and the temperature returned to normal. The partial tonsillectomy, by narrowing the orifices of the crypts of the remaining portion of the tonsil, favored the retention of bacteria and pathological detritus and made the conditions more favorable for a general infection.

The end-results of 1000 tonsillectomies performed during the past five years at the Johns Hopkins Hospital have been carefully studied. These operations were performed under the rigorous routine of a surgical ward, with experienced anesthetists and assistants, and were regarded as major surgical operations. The cases were followed up in order to learn the subsequent history of disorders supposed to be secondary to a chronic focus of infection in the upper air passages.

In the "arthritis group" four classes of cases are recognized: (1) infectious arthritis; (2) myalgia; (3) rheumatoid arthritis; (4) acute rheumatic fever.

1. *Infectious Arthritis.* Tonsils and adenoids were removed in 91 cases. The ultimate result was noted in 31. In 24 the joints are normal; 4 are improved although the joints have never entirely cleared up; 2 are not improved; 1 is worse than at the time of operation.

2. *Myalgia.* Four cases were followed up after tonsillectomy. All are well.

3. *Rheumatoid Arthritis.* Nine cases were followed up. Only 2 are improved; 2 are not improved, but no new joints are involved; 5 cases are much worse.

The conclusion drawn from this group of cases is that only in very exceptional circumstances should one subject a patient with rheumatoid arthritis to an operation for the removal of tonsils. These patients are for the most part middle-aged people. Their disease is well advanced when they seek medical advice. There is often marked anemia and a distinct lessening of their ability to withstand pain. After such a trying operation as tonsillectomy it often requires many weeks or months before the patient regains the physical condition present at the time the tonsillectomy was performed.

4. *Acute Rheumatic Fever.* Twenty-five cases were followed up; 4 of these cases had a recurrence, 1 of which had been perfectly well after the removal of his tonsils.

It is quite evident that the tonsils are not the only portal of entry for the organisms that cause rheumatic fever.

Opinions of Orthopedic Surgeons. With a view to ascertaining the opinion of medical men who have an exceptional opportunity of studying cases of arthritis a series of questions was submitted to 177 orthopedic surgeons throughout the country.

The questions called for answers with definite figures and not for opinions or beliefs.

The replies show the trend of present medical thought. They also show that a large percentage of orthopedic surgeons replying to the questionnaire believe that the removal of so-called foci of infections in teeth and tonsils have produced improvement and cure in many cases of acute and chronic arthritis. The beneficial results are more evident in acute than in chronic arthritis. If removal of foci in the teeth and tonsils does not bring about improvement the majority of these surgeons depend upon general hygienic or stimulative treatment. A small percentage continue the search for other foci, with special reference to the gastro-intestinal tract. It is interesting to note that opinion as to the accuracy of the statement that most foci of infection are to be found in the head is equally divided.

STATISTICS OF THE WRITER'S CASES. For several years the writer has conducted an investigation of the relation of diseased conditions of the teeth and tonsils to arthritis. The study was made in collaboration with dentists and ear, nose and throat surgeons, and included both hospital and private patients.

It was determined at the outset to leave the diagnosis and treatment of dental and tonsillar conditions entirely to the judgment of these specialists and to abide by their decision in each case. The results were determined by the patients' statements and by examination as to general health and condition of the joints. It was attempted to ascertain if operations on the teeth and tonsils had produced in the joints:

1. Cure.
2. Relief of symptoms.
3. No improvement.
4. Aggravation of symptoms.

Whenever possible the patients were referred back to the special surgeon for reexamination and after treatment following any operative procedure.

It is often impossible to determine what element in the treatment is responsible for the improvement or cure. Appropriate treatment for arthritis was instituted at the time the mouth and throat condition was being investigated and treated. When improvement is no more rapid than has been noticed for years under approved treatment for arthritis it is natural to attribute the progress to the true and tried methods.

Total number of cases, 40.

1. Diseased conditions of the teeth and tonsils, 29 cases: Of these (a) 12 were of the teeth alone; (b) 11 were of the tonsils alone; (c) 6 were of both teeth and tonsils.

2. Negative dental and nose and throat conditions, 8 cases: Of these 3 improved under treatment for arthritis; 2 were unimproved under treatment for arthritis; 3 could not be traced.

3. Dental and nose and throat examinations were not made in 3 cases: Of these 1 improved under treatment for arthritis; 2 could not be traced.

1 (a) Diseased conditions of the teeth alone, 12 cases: Of these 3 showed some improvement in the arthritis; 1 showed striking and immediate improvement; 3 improved after an interval of time had elapsed (1 of these last after several doses of autogenous vaccine); 2 were unimproved, all after the extraction of teeth; 1 was unimproved after a pyorrhea had been treated; 1 improved without operation; 1 could not be traced.

1 (b) Diseased conditions of the tonsils alone, 11 cases: Of these 2 were improved after tonsillectomy (1 of these was cured); 1 was unimproved after tonsillectomy; 1 was unimproved without tonsillectomy; 1 began to improve before tonsillectomy was performed; 1 was worse after tonsillectomy; 1 had a relapse after a tonsillectomy performed one year before; 1 refused operation.

1 (c) Diseased conditions of both teeth and tonsils, 6 cases: Of these 1 improved after extraction of teeth but relapsed later; 1 improved without operation; 1 was unimproved after extraction of teeth; 1 was unimproved after extraction of teeth and tonsillectomy; 1 was unimproved where operations were not performed; 1 refused operation.

In analyzing the above cases it will be seen that there was but one case which showed immediate improvement, which could be classed as a cure, following extraction of teeth, and but one such result following tonsillectomy.

Many of these cases which are classed as improved showed the improvement in their general health rather than in a changed appearance of the joints. It has seemed fair to consider them as better even if the improvement were slight.

In these few cases the improvement following proper treatment of dental disease was more noticeable than the improvement following operations on diseased tonsils.

In speaking of the above cases as improved or unimproved, either with or without operations on the teeth or tonsils, it is not implied that the operation, or the lack of operation, is responsible for the present condition of the patient. Many factors influence the result, and it is intended merely to state the condition of the patient when last seen.

As has been noted by others, diseased conditions of the teeth have been found more often in adults and diseased conditions of the tonsils more often in childhood.

SUMMARY. The relation of the teeth and tonsils to arthritis is at present a moot question. Billings and his followers point to the careful work of Rosenow and others on the bacteriology of arthritis and to the numerous cases of improvement and cure of arthritis following removal of diseased teeth and tonsils. They believe that

this proves the accuracy of their contention that a focus of infection exists in the head in many of these cases. On the other hand, many trained pathologists and reputable clinicians have been unable to reproduce either the laboratory findings or the clinical results of the Chicago workers. Consequently they either reject the theory as a whole or accept it in a greatly modified form. It is probable that the pendulum has swung too far in the direction of the wholesale removal of teeth and tonsils. The truth will probably be found in a middle ground somewhere between these divergent theories.

There is undoubted improvement in numerous cases of arthritis following the removal of an abscessed tooth or a diseased tonsil or when a case of active pyorrhea has received proper treatment. On the contrary, many such cases are given similar careful treatment without affecting the progress of the joint condition in the slightest degree.

One reason for the failure to obtain successful results in arthritis by treatment of dental and tonsillar disease is that the cases have been selected without knowledge of the exact pathological condition present in the organ in question. Many apical abscesses in which nature had effected a cure by walling off the disease have been treated by extraction of teeth. This has resulted not only in the loss of valuable teeth, but has at times been the cause of a dissemination of the infection to other parts of the body, with dire results.

In the same way the crypts in certain areas of a tonsil may overcome an existing infection. These crypts are perfectly harmless. A tonsil in which the crypts are sealed over by scar tissue, perhaps as the result of an incomplete tonsillectomy, may be a source of potent danger if the crypts contain an active focus of infection.

Success in treatment of these foci lies with the men who can distinguish the apical abscess and the diseased tonsil which are overcoming their infection by nature's methods. They must know by careful and special training when a tooth or a tonsil are active agents of infection. Such knowledge must be supplemented by accurate interpretation of dental roentgenograms and skilful laboratory work. Trite as the saying is, coöperation in such endeavor is the keynote of success.

Another reason for failure to alleviate arthritic cases is due to the fact that the focus of infection lies in some other part of the body. It may be discovered by further careful search in the lungs, heart, kidneys, genito-urinary or gastro-intestinal tracts, ductless glands, the nervous system and elsewhere. A certain number of cases are due to syphilis and to tuberculosis. Unfortunately in many cases it is never brought to light.

Many cases of arthritis are believed by thoughtful physicians to be due not to a localized collection of microorganisms but to an entirely different etiology. This class of cases is supposed to result from some disturbance of the metabolism, probably chemical in nature, which produces joint changes not always to be distinguished

from those caused by bacterial agency. They compose a fairly large share of the cases of chronic progressive arthritis seen in the daily routine of practice. A general flaccidity of tissues and relaxation of important organs accompanied by ptosis of the abdominal viscera often characterize these cases.

In acute arthritis the probability of producing a cure or improvement by the removal of a supposed focus in the teeth or tonsils is greater than in cases in the chronic stage. It is unreasonable to suppose that a restoration of function can be brought about in joints where extensive pathological changes have taken place.

One very suggestive fact brought out in this investigation has been the marked improvement in the general health of the patients when diseased conditions of the teeth and tonsils have been properly treated. It oftentimes seems as if a millstone had been removed from their necks. This is noted very commonly even when no change was apparent in the joint condition.

EXPERIMENTAL LESIONS IN THE CERVICAL SYMPATHETIC GANGLIA IN RELATION TO EXOPHTHALMIC GOITER.¹

By LOUIS B. WILSON, M.D.,

ROCHESTER, MINNESOTA.

THAT exophthalmic goiter, the clinical manifestations of which are due essentially to a greatly increased protein metabolism, is the joint result of disturbance in the several glands concerned with metabolism there can be little doubt. The fact that the thyroid shows a pronounced and constant series of functional changes parallel with the course of the disease and the further fact that removal of the gland arrests the symptoms is convincing though not absolute proof that the thyroid is the secretory gland the hyperfunction of which initiates the metabolic disturbance.

But is the primary hyperfunction of the thyroid the result of primary pathological change within the gland itself or of direct stimulation from its nerve supply? Cannon's² experimental production in cats of some of the symptoms of exophthalmic goiter by continuous stimulation of the thyroid through the sympathetic system suggests the latter. Durante and I³ have shown that in all

¹ Presented before the Association of American Physicians, Atlantic City, N. J., May 3, 1917.

² Cannon, W. B., Binger, C. A. L., and Fitz, R.: Experimental Hyperthyroidism, *Am. Jour. Physiol.*, 1914-15, xxxvi, 363-364.

³ Wilson, L. B., and Durante, L.: Changes in the Superior Cervical Sympathetic Ganglia Removed for the Relief of Exophthalmos, *Jour. Med. Research*, 1916, N. S., xxxiv, 273-296. Wilson, L. B.: The Pathological Changes in the Sympathetic System in Goiter, *Am. Jour. Med. Sc.*, 1916, clii, 799-812. Wilson, L. B.: Further Study of the Histopathology of the Autonomic Nervous System in Goiter, *Jour. Lab. and Clin. Med.*, 1917, ii, 295-307.

cases of exophthalmic goiter we have had an opportunity to examine there is a pronounced and constant pathological lesion in the cervical sympathetic ganglia from which the thyroid receives its entire nerve supply. There is much suggestive evidence that these pathological changes in the cervical sympathetic ganglia are the result of direct bacterial infection within the ganglia.

The object of the present series of experiments has been to determine the effect directly upon the cervical sympathetic ganglia and indirectly upon the thyroid of various forms of stimulation applied to the ganglia themselves in healthy animals. Goats have been used for the experiments almost exclusively, and the results on these animals only will be described herein. The goat is a very desirable animal for experiments on the sympathetic ganglia and the thyroid, since the tissue elements of both these organs in their normal and pathological morphology and their staining reactions closely resemble those of the tissue elements of the same organs in man.

Stimulation in some of the experiments has been produced by electricity; in most instances, however, the stimulus has been obtained by direct bacterial inoculation into the ganglia. Observations have been completed on nineteen goats, and are still in progress on six others.

TECHNIC. Electric Stimulation. After proper etherization of a goat its right superior cervical sympathetic ganglion was exposed. The ganglion was then directly stimulated by a moderate tetanizing current for one second, at intervals of three seconds, for a period of one hour. During the experiment the animal's blood-pressure was taken and the amount of saliva excreted noted. After one hour the right cervical ganglion and the right lobe of the thyroid were removed with as little loss of blood as possible. The left superior cervical sympathetic ganglion was then exposed and stimulated in the same manner as the right had been, but for a period of five and a half hours. At the end of five and a half hours the left superior cervical sympathetic ganglion and the left lobe of the thyroid were removed. After removal the ganglia and the lobes of the thyroids were properly fixed and stained by various methods, the ganglia usually by Nissl's and Ramon y Cajal's methods and the thyroid with hematoxylin-eosin and by Bensley's acid-fuchsin-methylene-green after acetic-osmic-bichromate fixation.

Bacterial Stimulation. After properly etherizing a goat its right or left superior cervical sympathetic ganglion was exposed and a small quantity of a culture of some bacterium was injected into the capsule of the ganglion. The wound was closed with aseptic precautions and the goat placed under observation. The period of observation varied from three days to three months. A few of the animals died and in such instances complete postmortems were made. In some of the others the cervical sympathetic ganglia and the lobes of the thyroid from both sides were removed at oper-

ations. In the remainder of the goats only the injected ganglion and the thyroid lobe on the same side were removed and examined.

SUMMARY OF OBSERVATIONS. 1. The normal nerve cells of the cervical sympathetic ganglia in the adult goat closely resemble the normal nerve cells of the cervical sympathetic ganglia of the human adult, except that a relatively large number of them are binucleate. Similarly, the thyroid of the adult goat when at rest histologically closely resembles the resting adult human thyroid.

2. (a) Moderate electrical stimulation applied for one second at intervals of three seconds for a period of one hour to the superior cervical sympathetic ganglion of an adult goat appears to produce no marked changes in the blood-pressure or respiration. If there were any definite changes they were masked by the diffuse stimulation involving the vagus. There was marked salivation.

(b) Microscopically, after the electrical stimulation noted above a large number of the nerve cells of the stimulated ganglion were swollen and showed hyperchromatization. The demonstration of dissolution of the chromatin by Nissl's method or of the presence of lipoid changes by Sudan III and Ramon y Cajal's methods has not been possible in any of the cells.

(c) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen, their protoplasm distinctly granular and their nuclei well rounded. The acini were distended with a feebly staining secretion, the numerous large vacuoles in stained preparations of which indicated the liquid character of the secretion. The condition of the cells and colloid secretion was parallel in all respects to that found in the thyroids of early cases of exophthalmic goiter in the human subject.

3. (a) Moderate electrical stimulation applied to the superior cervical sympathetic ganglion for one second, at intervals of three seconds, throughout a period of five and a half hours, produced clinical changes similar to those noted in Paragraph 2.

(b) Microscopically, after the electrical stimulation noted above, many of the nerve cells were markedly swollen and showed intense hyperchromatization. Many were swollen, hydropic and with disseminated chromatin. Sudan III preparations, even when thoroughly differentiated, showed conclusive evidence of lipoid change. This was demonstrated by Ramon y Cajal's method.

(c) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen but not nearly so much so as in those thyroids in which stimulation had been applied for only one hour. The protoplasm was clear and the nuclei showed a tendency to crenation. The acini were usually more distended and were filled with colloid material, which was more densely stained and contained fewer vacuoles than that noted in Paragraph 2 (b). These changes were evidently the result of beginning exhaustion of the cells and resembled the changes in the thyroid in cases of exophthal-

mic goiter in the human subject in which remission of symptoms has already begun.

4. (a) After the injection of a virulent culture of *Streptococcus hemolyticus* into the capsule of the superior cervical sympathetic ganglion of goats the animals died within three days after exhibiting symptoms of an intense toxemia.

(b) Within the injected ganglion of such a goat the nerve cells were found to lie in greatly distended pericellular lymph spaces. They were markedly hyperchromatic and hydropic, with diffuse dissemination of the chromatin, or were more or less completely disintegrated. No evidence of lipid change was demonstrated by the Sudan III or silver-impregnation methods.

(c) After the above injection the cells of the thyroid parenchyma were palely staining, not swollen and apparently not overfunctioning. The amount and character of the colloid within the acini was not distinguishable from normal.

5. After the injection of certain strains of *Bacillus influenzae* of apparently low virulence no systemic reaction or histological lesions were demonstrated. After the injection of other strains more recently isolated a marked inflammatory reaction was found around the injected ganglia, though the goats had shown no symptoms. Changes within the ganglia and within the thyroid were indistinguishable from those within the ganglia and thyroids from the goats described in Paragraph 6.

6. (a) The injection of freshly isolated virulent cultures of *Bacillus bronchisepticus* into the superior cervical sympathetic ganglion of adult goats usually produced marked constitutional symptoms such as trembling, increase of temperature, and loss of appetite, and frequently caused death in from three days to three weeks. No exophthalmos was noted.

(b) Within the injected ganglion of such a goat many of the nerve cells in animals dying early were found to be markedly hyperchromatic; others were hydropic, with disseminated or invisible chromatin and more or less distorted nuclei within such cells. Sudan III and silver-impregnation preparations showed the presence of changed lipoids. In the ganglia of goats that lived three weeks or more there was unmistakable evidence of complete cell destruction, in some instances extending from the point of inoculation well into the ganglion. Lipoid pigmentation was distinctly shown by Sudan III and silver impregnation. Histologically, these changes were parallel to those found in the ganglia in cases of exophthalmic goitre in the human subject.

(c) In goats from which the thyroid had been removed in from three days to three weeks after the injection the cells of the thyroid parenchyma were actively functioning, as was evidenced by their swollen size, granular protoplasm, well-rounded nuclei and the presence of large quantities of feebly staining secretion within the

acini. The histological appearance was closely parallel with that found in the thyroid in early cases of exophthalmic goiter. When a period of three months had elapsed between inoculation and removal of the thyroid the thyroid parenchyma showed evidence of exhausted function in that the cells were no longer swollen, their nuclei were more or less crenated and the colloid secretion within the acini was densely staining.

CONCLUSION. From the above experiments it would appear that irritation from the presence of certain bacteria within the cervical sympathetic ganglia of the goat may produce histological pictures within the ganglia and in the thyroid which parallel those found in the various stages of progressive and regressive exophthalmic goiter. This evidence supports the suggestion that in exophthalmic goiter the thyroid receives its stimulus to over-function through its nerve supply and as a result usually of a local infection in the cervical sympathetic ganglia.

A STATISTICAL STUDY OF THE RELATIONSHIP OF THE ORIGIN OF ECTOPIC CONTRACTIONS TO VENTRICULAR PREPONDERANCE AS SHOWN BY THE ELECTROCARDIOGRAPH.¹

BY ARTHUR E. STRAUSS, S.B., M.D.,

ST. LOUIS, MISSOURI.

THAT the form of the electrocardiogram may indicate relative ventricular preponderance has been known for some time, but the relationship of such preponderance to the origin of ectopic contractions has, so far as we are aware, never been made a subject of study. Is it not possible that there may be some underlying relationship between preponderance and ectopic contractions that has escaped our attention up to the present?

It was with this possibility in mind that we began the review of the 375 cases studied by means of the electrocardiograph within the past eighteen months. The study was made in the cardiographic laboratory of the University of Pittsburgh, School of Medicine, at St. Francis Hospital. Most of the electrocardiograms were taken on patients who presented some cardiac disturbance, although a few were taken on patients in whom no cardiac lesion was suspected.

In the determination of preponderance we have used the criteria of Lewis,² slightly modified. Lewis, following the teachings of

¹ R. B. Mellon Fellow in Internal Medicine, University of Pittsburgh, School of Medicine, Pittsburgh, Pa.

² Clinical Electrocardiography, Shaw & Sons, London, 1913. Observations upon Ventricular Hypertrophy, with Special Reference to Preponderance of One or Other Chamber, Heart, 1914, No. 4, v, 367-402.

Einthoven,³ believes that those curves which show the deepest deflection in lead I and the tallest summit in lead III indicate a relative preponderance of the right ventricle. The reverse of this picture—namely, the tallest summit in lead I and the deepest in lead III—is taken by him as indicative of preponderance of the

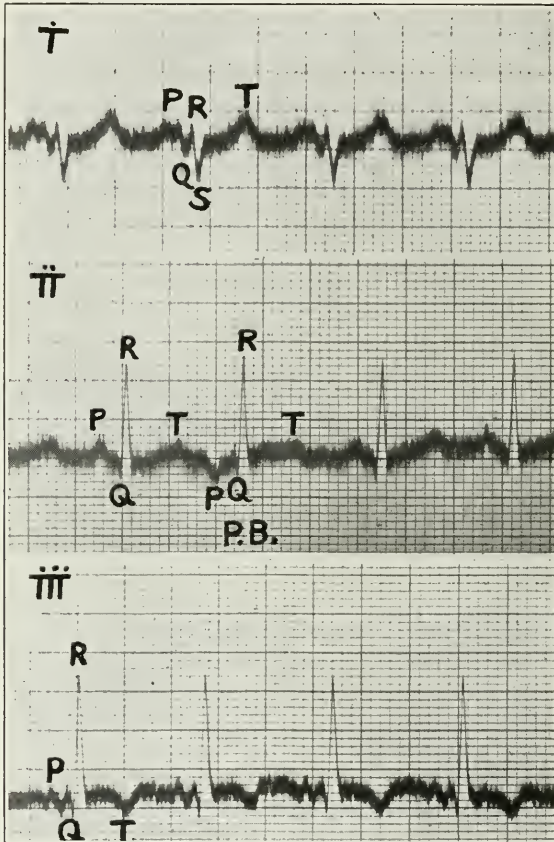


FIG. 1 (No. 289-2, leads I, II, III).—Electrocardiogram illustrating right ventricular preponderance. The *S* wave is deepest in lead I and the *R* wave is highest in lead III. This figure also illustrates a typical auricular premature contraction, in which the *P* is inverted and the ventricular complex unchanged. There is no compensatory pause following the premature beat.

left ventricle, in which case there is a prominent *R* in the first lead accompanied by a diminutive *R* and exaggerated *S* in lead III. The modification used consisted merely in the inclusion in our statistics of those cases in which either *R* II or *S* II were greater than the corresponding waves in leads I or III, but in which consider-

³ Arch. Internat. de Physiol., 1906, iv, 132; Arch. f. d. ges. Physiol., 1908, cxxii, 517 (quoted by Lewis).

ing leads I and III only there was a marked convergence of the *R* and *S* waves in cases of right ventricular preponderance and a marked divergence in cases of left ventricular preponderance.

Of the 375 cases studied, 136, or 36.2 per cent., showed left ventricular preponderance; 37 cases, or 9.8 per cent., showed right ventricular preponderance; while 202 cases, or 53.7 per cent.,

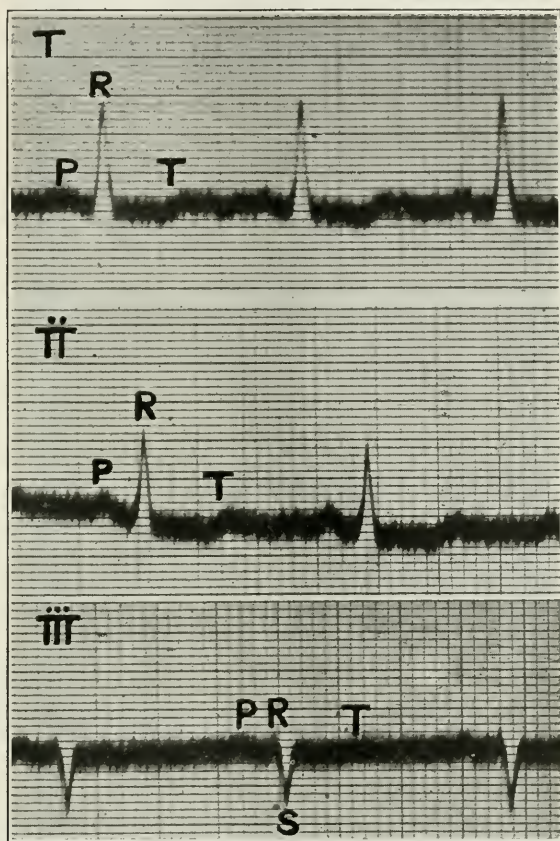


FIG. 2 (No. 359-1, leads I, II, III).—Electrocardiogram illustrating left ventricular preponderance. The *R* wave is highest in lead I and the *S* wave is deepest in lead III.

showed no relative preponderance. An apparent change in preponderance was noted in 8 cases, or 2.1 per cent., of which 2 showed a transition from left to right, or *vice versa*, 1 from right preponderance to no preponderance, or *vice versa*, and 5 from left preponderance to no preponderance, or *vice versa*.⁴ Two other cases showed a doubtful

⁴ Some of these changes may have been due to change of position of the patient, as often many e'grams were made on the same case and no separate record was kept of those e'grams taken in the upright and reclining postures.

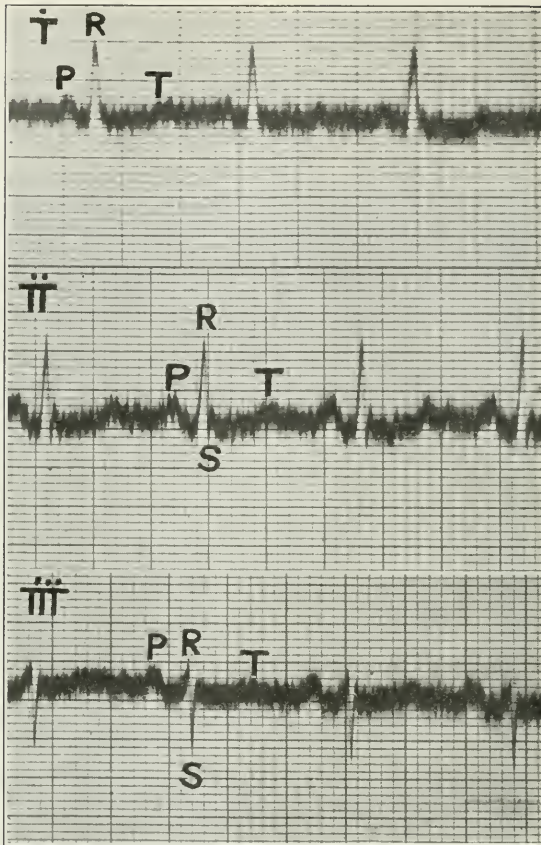


FIG. 3 (212-1, leads I, II, III).—Electrocardiogram not strictly fulfilling Lewis's criteria but representative of the type of case included in our modification as showing left ventricular preponderance. Note the *R* wave of lead II is higher than that of lead I, but the divergence of the *R* and *S* waves of leads I and III respectively is marked.

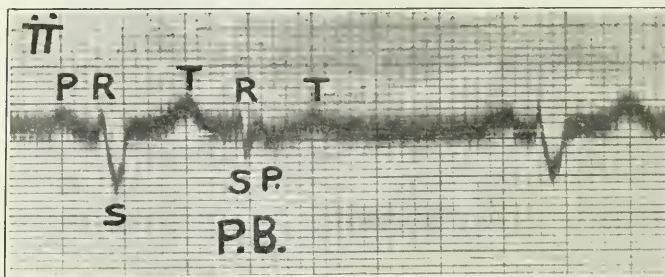


FIG. 4 (No. 210-10a, lead II).—Electrocardiogram illustrating a premature contraction arising in the auriculoventricular tissues. A low origin in the junctional tissues is indicated by the *R-P* sequence.

transition, but, as in the case of all figures in this paper, these doubtful cases were not included in the compilation of the statistics.

The relationship of the origin of ectopic beats⁵ to ventricular preponderance forms the main theme of this study. The three types of ectopic contractions are: (1) auricular, (2) junctional and (3) ventricular. The latter may be further subdivided into those

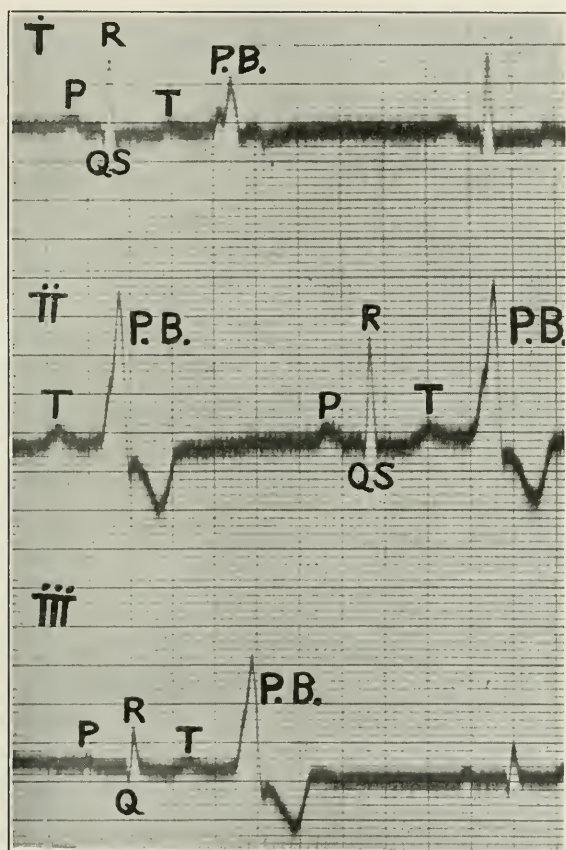


FIG. 5 (No. 149-14, leads I, II, III).—Electrocardiogram illustrating premature contractions arising in the right ventricle. The electrocardiogram also shows an absence of relative ventricular preponderance.

arising in the apical or left ventricular region and those arising near the base or right ventricle. We are not able at the present time to determine whether the ectopic beats arising in the auricle come from the left or right side, and although we know the relative position of beats arising in the atrioventricular tissue, that differentiation will

⁵ We use the terms ectopic and premature and contractions and beats interchangeably in this paper.

not be considered in this communication. The characteristics of the several types of premature contractions need not be repeated here, as they are thoroughly familiar to everyone acquainted with the subject of electrocardiography and others will find a simple account in Lewis's book on *Clinical Electrocardiography*. The determination of the origin of ectopic beats is usually very simple, the

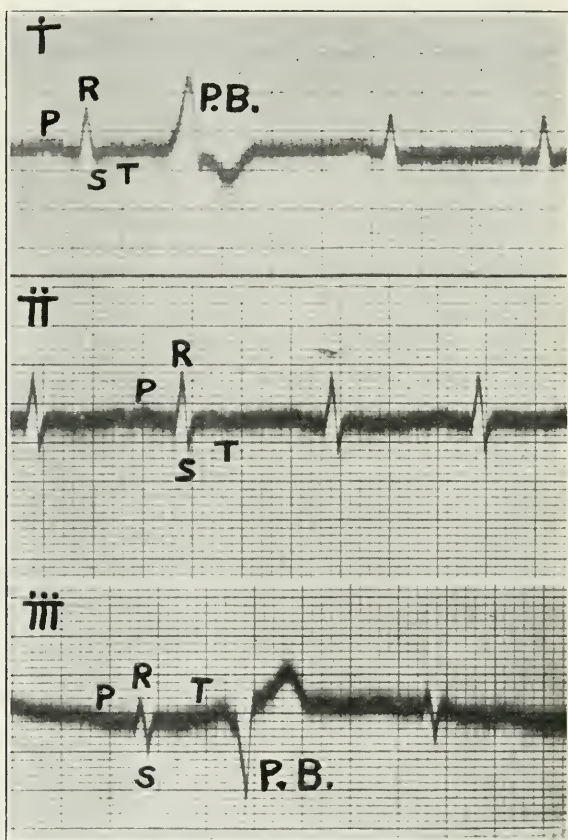


FIG. 6 (No. 130-1, leads I, II, III).—Electrocardiogram illustrating premature contractions arising in the left ventricle. The premature beats are shown in leads I and III only.

single difficulty often encountered being in the differentiation of ventricular beats of right and left origin when occurring only in lead I. In but 2 instances in our series did such premature contractions occur only in lead I, and these 2 cases were of the typical form of those of left ventricular origin, and are therefore included in the study.

Premature contractions (P. B.'s) of one type or another occurred 76 times (20.2 per cent.) in the 375 cases studied. Although it is

generally stated that an individual case usually shows but one type of premature beat, we found in our series 11 cases, or 17.4 per cent., which showed two different types, of which cases 2, or 3.2 per cent., showed ectopic beats arising in three different foci. Subtracting those cases counted twice or thrice we found ectopic beats in 63 different cases, or 16.8 per cent. of the series.

TABLE 1.

		Per cent.
Cases showing left ventricular preponderance	136	36.5
“ right ventricular preponderance	37	9.8
“ no ventricular preponderance	202	53.7
Total number of cases in series	375	100.0
Cases showing left ventricular P. B.'s	30	8.0
“ right ventricular P. B.'s	25	6.6
“ auricular P. B.'s	11	2.9
“ junctional P. B.'s	10	2.6
Total all cases of P. B.'s	76	20.1

A glance at Table I will show that premature beats arising in the left ventricle are the most common, with right ventricular premature beats running a close second. Next in order of frequency come auricular and junctional premature contractions which, in our series, occur in almost equal number. Ectopic beats of ventricular origin arising in both apical and basilar regions together are about five times more frequent than either auricular or atrioventricular premature contractions.

Can we analyze these cases further? Is there a causative relationship between preponderance and origin of ectopic beats? In an attempt to answer that question we present the following summary:

4 cases or 2.9 per cent. of left ventricular preponderance show auricular P. B.'s
1 case or 2.7 per cent. of right ventricular preponderance show auricular P. B.'s
6 cases or 3.0 per cent. of no preponderance show auricular P. B.'s
<hr/>
Total 11 cases or 2.9 per cent. of all cases show auricular P. B.'s
7 cases or 5.1 per cent. of left ventricular preponderance show junctional P. B.'s
0 cases or 0.0 per cent. of right ventricular preponderance show junctional P. B.'s
3 cases or 1.5 per cent. of no preponderance show junctional P. B.'s
<hr/>
Total 10 cases or 2.6 per cent. of all cases show junctional P. B.'s
13 cases or 9.5 per cent. of left ventricular preponderance show right ventricular P. B.'s
4 cases or 10.8 per cent. of right ventricular preponderance show right ventricular P. B.'s
8 cases or 3.9 per cent. of no preponderance show right ventricular P. B.'s
<hr/>
Total 25 cases or 6.6 per cent. of all cases show right ventricular P. B.'s
18 cases or 13.2 per cent. of left ventricular preponderance show left ventricular P. B.'s
1 case or 2.7 per cent. of right ventricular preponderance show left ventricular P. B.'s
11 cases or 5.4 per cent. of no preponderance show left ventricular P. B.'s
<hr/>
Total 30 cases or 8.0 per cent. of all cases show left ventricular P. B.'s

But brief comment is necessary, as the summary tells its own story. Auricular premature contractions occur in practically equal proportion in all types of preponderance. A greater percentage of left ventricular preponderance show junctional premature beats. Right ventricular premature beats occur in the largest percentage

in cases showing right ventricular preponderance while left ventricular premature beats occur in the largest proportion of left ventricular preponderance. As this data is based on the relative as well as the absolute proportions of these phenomena it is not unreasonable to suspect an underlying cause. A possible explanation seems to be that the hyperactivity or other abnormal conditions present in that portion of the heart that gives rise to the electrical phenomena of preponderance may likewise cause it to have an increased irritability and therefore more prone to be the seat of origin of ectopic beat formation. The series presented in this study, however, is comparatively small and the difference in relative frequency of right ventricular premature beats in cases showing right and left preponderance so little that one cannot be too cautious in drawing conclusions.

SUMMARY. In a study of 375 cases 36 per cent. showed evidence of left ventricular preponderance and 10 per cent. showed evidence of right ventricular preponderance, while 2 per cent. showed an apparent change in preponderance at different times and under varying conditions.

Premature contractions of all types occurred 76 times in the series of 375 cases (20 per cent.). In the 63 individual cases showing premature beats, 11, or 17 per cent., showed at least 2 different types while 2 cases showed origin in 3 different foci. Left ventricular premature beats were most frequent, right ventricular, auricular and junctional contractions occurring next in order in diminishing frequency.

The greatest percentage of right ventricular preponderance showed right ventricular premature contractions, while the largest percentage of left ventricular preponderance showed ectopic beats arising in the left ventricle. From these facts there is deduced a possible etiological theory to account for the relationship of preponderance and the origin of ectopic beats.

STUDIES IN CHOLELITHIASIS.

III. THE IMMEDIATE EFFECT OF THE VARIOUS TYPES OF OPERATIONS UPON THE CHOLESTERINEMIA.

BY ABRAHAM O. WILENSKY, M.D.,

AND

MARCUS A. ROTHSCHILD, M.D.

NEW YORK.

(From the Pathological Laboratory of Mount Sinai Hospital.)

IN the second paper of this series it was shown that a proper conception of the underlying pathological disturbance, initiating

disease of the bile passages with stone formation, was only possible in the light of the cholesterin content of the blood after exact knowledge was obtained of actual anatomical conditions. The next stage of the study directed itself, naturally, toward an investigation of the effect which the various types of operation had upon these conditions, especially the effect upon the underlying metabolic disturbance when the latter was present. As a basis for this part of the study there are the variations in the cholesterinemia determined by frequent estimations of the cholesterin content of the blood after operation and the correlation of these with the clinical histories.

It was soon found, however, that in a certain number of the patients the immediate effect differed from the ultimate one observed when the cases were followed over long periods of time. This necessarily complicates matters considerably, and therefore, for a matter of convenience, we have restricted ourselves to giving in this communication only those effects which were seen to follow immediately after operation.

The operations employed at Mount Sinai Hospital are the usual ones made use of in any surgical clinic and given in the order of frequency of their performance are as follows:

1. Cholecystectomy.
2. Cholecystectomy with drainage of the cystic duct.
3. Cholecystectomy with drainage of the hepatic duct through the cystic duct.
4. Cholecystectomy and choledochotomy with drainage of the common bile duct.
5. Cholecystostomy with drainage of the gall-bladder and rarely with choledochotomy and drainage of the common bile duct.
6. Cholecystotomy.

In the classifications hereinafter given we have considered 2 and 3 as accomplishing the same purpose and have therefore grouped them together. The effect of cholecystotomy will not be considered, as we have studies so far in only one case.

These operations were performed on the surgical services of Drs. Lilienthal, Beer, Berg, Elsberg and Moschcowitz, either by themselves or by their associates. We are indebted to all of them for the privilege of carrying on these studies and for their kind coöperation.

In the following tables the variations in the cholesterin content of the blood after each type of operation are given. In each case the interval after operation is noted; also whether any complication such as obstruction had been present.

When estimations are made shortly after this type of operation the variations in the figures are not marked. Many of the differences could be accounted for as being within the limits of personal error. When the observations are made somewhat later, that is at about

the end of the second or third weeks, one finds a moderate drop in the amount of blood cholesterin. The decrease has usually averaged about 50 mg. of cholesterin per each 100 c.c. of blood. When the differences are marked there had always been a preëxisting obstruction of the common bile duct which had been relieved by operation.

TABLE I.—CHOLECYSTECTOMY: NO BILE DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.	Remarks.
267	0.125	0.125	13	
284	0.162	0.172	4	
260	0.209	0.125	18	Jaundiced
166	0.190	0.158	14	
181	0.110	0.125	4	
312	0.125	0.1525	6	
306	0.190	0.170	15	
433	0.172	0.162	5	
169	0.155	0.110	15	
382	0.175	0.115	12	
195	0.176	0.162	5	

When the postoperative variation in the cholesterin content of the blood has been a slight rise rather than a diminution we have accounted for the discrepancy in either of two ways: (1) as being within the limit of personal error, or (2) as being due to obstruction in the ducts caused by a temporary inflammatory swelling of the wall structures resulting from the operative trauma.

TABLE II.—CHOLECYSTECTOMY WITH CYSTIC OR HEPATIC DUCT DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
270	0.155	0.140	14
294	0.205	0.195	52
222	0.176	0.162	25
145	0.175	0.172	5

The postoperative variations in the cases in this group are very similar to those in the previous one. Case No. 294 was frequently jaundiced, but this had disappeared a few days prior to operation.

TABLE III.—CHOLECYSTECTOMY WITH COMMON DUCT DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
235	0.190	0.161	14
163	0.235	0.175	7
343	0.242	0.275	6
264	0.200	0.125	24
127	0.237	0.137	6
147	0.212	0.125	15

When the common bile duct is drained the postoperative drop is very marked. In case No. 343 it was noted at the time of operation that there was a marked inflammatory stricture of the common duct secondary to a gangrenous empyema of the gall-bladder. The operative trauma evidently intensified this and accounted for the postoperative increase in the cholesterin content of the blood. Later, when this subsided, the obstruction was relieved spontaneously, and then the cholesterin content of the blood fell to 0.14 mg. per cent.

TABLE IV.—CHOLECYSTOSTOMY WITH GALL-BLADDER DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cen.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
202	0.212	0.185	15
177	0.220	0.1465	10
94	0.150	0.126	8
384	0.207	0.190	5
151	0.215	0.140	6
119	0.237	0.145	8
126	0.200	0.125	6
134	0.290	0.155	7
106	0.2725	{ 0.1665	3
		{ 0.16675	9
177	0.220	{ 0.1415	3
		{ 0.0837	27

These cases show a similarity to those in which a cholecystectomy is performed and the common bile duct is drained. The fall in the cholesterin content of the blood is always large and immediate.

DISCUSSION. The performance of any of these operations immediately produces new conditions which have a variable influence on the metabolic activities of the cholesterin metabolism, and upon its index the cholesterin content of the blood. These conditions may be considered as owing their existence:

1. To the preparation of the patient for operation.
2. To conditions produced by the operation itself.
3. To conditions in the early postoperative period.

More in detail the preparation for operation includes:

1. A short period of starvation.
2. Active catharsis.

The period of food deprivation removes for the time being an important source of intake for the cholesterin content of the body. The active catharsis removes from the bowel the accumulation of cholesterin and cholesterin esters derived from the bile, which, under the usual conditions, would be reabsorbed into the lymphatic system. Both of these combined subserve the same purpose while functioning in diverse ways and accomplish a diminution in the cholesterin content of the body. Inasmuch, however, as these factors are only operative for a short period of time, rarely over twelve to twenty-four hours, the actual result accomplished, as

indicated, in the cholesterol content of the blood is hardly appreciable.

The operative attack necessarily entails:

1. The giving of an anesthesia, usually nitrous oxide gas, followed by ether, very rarely with the addition of small quantities of chloroform.

2. A loss of blood which only exceptionally is large enough to be recognizable in its effects and may therefore be disregarded as inconsequential.

3. A certain degree of insult to the sympathetic nervous system; and in certain instances it accomplishes

4. The drainage of bile from the biliary passages.

The pharmacological action of the various drugs employed as anesthetics is of the depressing variety, and although no special studies have been made upon the effect of these drugs upon the cholesterol metabolism, one may safely assume that this, in common with other metabolic activities, will be diminished. The sympathetic nervous system is intimately connected with the adrenal glands and consequently with the cholesterol metabolism. A disturbance of the normal equilibrium which results from any operative attack will, to a certain degree, be reflected in the changes observed after operation in the cholesterinemia. When a biliary fistula is made the escape of bile diverts from the bowel those cholesterol bodies which normally form one of the important sources of derivation for the cholesterol content of the body. The total effect of all these combined would be indicated in a diminution of the cholesterol content of the blood.

The conditions accompanying the early postoperative period are:

1. The deprivation of food or a diet in which the lipid content is at a minimum.

2. A short period of constipation which occasionally becomes protracted.

3. The renal congestion consequent to the anesthetic, occurring very frequently, usually lasting only for a few days, but occasionally assuming the characteristics of a true nephritis.

4. The continuation of bile drainage when such a fistula has been established.

The deprivation of lipid material from the diet naturally lowers the cholesterol content of the body, although it should be remembered that the withholding of all food tends to increase the cholesterol content of the blood. Whenever a biliary fistula is present this diminution in the cholesterol of the body will be all the more enhanced. True nephritides are frequently associated with hypercholesterinemic states of the blood.

With the exception of the question of drainage the factors involved in preparing for operation and those relating to the operation itself

are practically identical for every patient and may be considered as constants. In any discussion therefore these will bear no influence upon the final result. Those factors relating to conditions after operation naturally vary with the individual patient. Of these the most important is the influence of bile drainage.

The escape of bile through a fistula established into the common bile duct is always complete for a variable length of time, but as inflammatory reactions subside a smaller or greater portion of bile will trickle down alongside of the tube into the duodenum. One frequently notices a slight coloring of the stools after a common duct fistula has been draining for some time, whereas, at first, these have been clay-colored. On the other hand the escape of bile through a gall-bladder fistula is complete only when there is associated some obstruction in the common bile duct. The two following cases illustrate this latter point.

CASE No. 106. In a forty-year-old woman attacks of cholecystitis with jaundice had occurred frequently during the previous eighteen months. At the operation a thin, slightly inflamed gall-bladder was found with stones and a cholecystostomy was made. The cholesterin estimations before operation and the changes occurring in the metabolism after operation are demonstrated in the following table:

TABLE V.—CASE NO. 106.

Date.	Blood cholesterin, mg., per cent.	Bile cholesterin, mg., per cent.	Biliuria.	Stool.
Preoperative:				
May 28	0.2725			
June 2	0.250			
Postoperative:				
June 4		0.100	None	Colored
5		0.100	"	"
6		0.075	"	"
7		0.067	"	"
8		0.134	"	"
10		0.120	"	"
11	0.16675	0.108	"	"
12		0.102	"	"
13		0.092	"	"
15		0.089	"	"
16		0.079	"	"

CASE No. 177. A fifty-year-old woman gave a history of repeated attacks of cholecystitis in the previous sixteen months without any jaundice. At the operation a thin-walled distended gall-bladder was found containing numerous small faceted stones and a cholecystostomy was done. The cholesterin estimation before operation and the variations occurring in the cholesterin content of the blood and bile after operation are shown in Table VI.

TABLE VI.—CASE NO. 177.

Date.	Blood cholesterin, mg., per cent.	Bile cholesterin, mg., per cent.	Biliuria.	Stool.
Preoperative:				
Sept. 15	0.220			
Postoperative:				
Sept. 24		0.091	None	Acholic
25	0.1415	0.085	"	"
26		0.0765	"	"
27		0.125	"	"
28		0.085	"	Colored
29		0.110	"	"
30		0.106	"	"
Oct. 1		0.0905	"	"
3		0.094	"	"
5		0.116	"	"
8		0.0825	"	"
12	0.0837	...	"	"

CASE No. 106 had no obstruction in the common duct. Relatively small amounts of bile escaped and the stools were well colored. The bile content of cholesterin was relatively within normal limits, indicating that sufficient quantities of cholesterin bodies were being reabsorbed from the intestinal tract to keep up the normal cholesterin content of the bile. The blood cholesterin fell only to the normal level. Case No. 177, for some reason had, immediately following the operation, some inflammatory obstruction in the common duct, as indicated by the clay-colored stools. (There was no bile in the urine and no jaundice, because all of the bile was escaping through the gall-bladder fistula.) The cholesterin content of both blood and bile, and especially the content of the blood, fell far below the normal level, indicating that the body was being depleted of its cholesterin. In both of these cases the food factor was constant, both of the patients being upon the same diet.

The effects of these two means of bile drainage may be summarized as follows:

1. With common-duct drainage the system is rapidly depleted of its cholesterin.

2. Gall-bladder drainage does not accomplish this extreme effect unless there be a concomitant obstruction in the common bile duct.

3. The rate of drop varies and depends upon the initial figure and the length of time of drainage. After a certain minimum is reached there is no further fall in the cholesterin content of the blood.

4. These effects are obtainable only when the operation has been so performed that proper bile drainage is accomplished and all obstructions have been removed from the ducts. This was most perfectly illustrated by the following case:

CASE No. 172. In a twenty-seven-year-old married woman three attacks of gallstone colic had occurred four months, six weeks and four days previous to admission to the hospital; the last two attacks were accompanied by slight degrees of jaundice. The patient was slightly jaundiced at the time of operation. At the operation (September 8) a normal-looking gall-bladder was found to contain small greenish-black stones and the hepatic and common ducts were apparently empty. A cholecystostomy was made. The contents of the gall-bladder were sterile bacteriologically.

On September 12 there was an attack of colic, with slight icterus, which entirely subsided by September 17. On September 26 the notes state that the discharge of bile from the fistula had been profuse, the fluid was turbid and green in color and a stone had been felt in the gall-bladder on the previous day. This was extracted on September 26. Up to October 12 the drainage, however, had continued to be just as profuse, and on the day following the bile passages were explored. A secondary cholecystectomy was done and a stone which was impacted in the papilla was extracted. The hepatic ducts were drained. The character of the bile drainage changed immediately and the color of the bile became clear golden yellow. The convalescence was uneventful thereafter. The cholesterin variations are indicated as follows:

TABLE VII.—CASE NO. 172.

Date.	Temp. ° Fahr.	Blood cholesterin. mg. per ct.	Bile cholesterin.			Biliuria.	Stool.
			C. c.	Sp. gr.	Mg. per cent.		
Preoperative:							
Sept. 6 . . .	99.8°	0.155					
Postoperative:					(G. B.)		
Sept. 8 . . .	100.0	0.117		
9 . . .	101.2	...	190	1010	0.061	None	Acholeic
10 . . .	100.4	...	140	1010	0.037	"	"
			70	1010	0.054	"	"
11 . . .	99.8	...	102	1010	0.0545	"	"
			88	1010	0.051	"	"
13 . . .	103.0	...	130	1010	0.0352	"	"
14 . . .	102.4	...	192	1010	0.022	"	"
15 . . .	100.2	...	122	...	0.0082	"	"
16 . . .	100.2	0.162	270	1008	0.031	"	"
17 . . .	99.2	...	275	1010	0.0205	"	"
18 . . .	99.2	...	470	...	0.0355	"	"
28 . . .	101.4	...	450	1010	0.031	"	"
29 . . .	99.4	...	530	1010	0.044	Trace	"
Oct. 1 . . .	99.0	0.165	None	"
14 . . .	101.8	...	111	1012	0.025	"	"
15 . . .	101.6	...	110	1010	0.034	"	Slight color
17 . . .	99.8	0.066	"	Colored
21 . . .	99.6	0.0475	"	Well colored
23 . . .	99.6	0.075	"	"
28 . . .	99.4	0.125	"	"

While studying this case we were impressed by the fact that the cholesterol content of the blood did not fall after operation to the level, to which ordinarily we were accustomed to see it fall, and we suspected that the bile passages were not absolutely free. It was only after the second operation, when the common bile duct was cleared, that we saw the cholesterol content of the blood fall to the expected low level. In several instances, occurring subsequently, we made use of this principle in making the diagnosis that the ducts had not been thoroughly cleared and were later much gratified to have our diagnoses verified.

The drainage of bile obtained by inserting a tube into the stump of the cystic duct is found practically to be of little effect. It usually happens that such a tube slips out of its proper position and then the drainage corresponds to the leakage which one so frequently sees after the cystic duct has been tied and the ligature has given way. In our experience this drainage is most ineffectual.

When a tube is inserted into one of the hepatic ducts the amount of bile escaping will produce the effects obtained by drainage of the gall-bladder. Our experience would practically lead us to say that it is an inferior method of drainage.

The effect of bile drainage *per se* upon the underlying metabolic activities whose function is the control of the cholesterol content of the body and blood is *nil*. What is accomplished is the removal of that portion of the cholesterol which exceeds the normal minimal content. How thoroughly this is accomplished depends upon the completeness or incompleteness of the biliary fistula, and, when this is complete, one may see the cholesterol content of the blood fall to values below the normal. The depleting effect of bile drainage may be enhanced or retarded by a lack of superabundance of lipid in the diet, and when a rapid depletion of cholesterol bodies is desirable it is of advantage to submit the patient to a lipid-free diet.

The loss of bile produced by a biliary fistula has a deleterious effect upon the animal body, and when this has lasted for an appreciable length of time, patients are liable to exhibit any or all of the following symptoms:

1. Disturbance of the digestive function frequently accompanied by vomiting.
2. Greater or less degrees of constipation induced by an absence of bile from the intestinal tract.
3. Depreciation in the general well-being and vigor of the body and a deterioration in the patient's general condition, as evidenced by an impairment in the circulation, in a lessened resistance to bacterial or other trauma and in a general lassitude and muscular weakness.

This deleterious effect may be counteracted or may be forestalled by collecting the biliary drainage and by feeding it after filtration

to the patient by stomach tube. Occasionally one meets with a patient who is able to drink the bile directly, and for this type of patient some of the obnoxiousness may be removed by the addition of salt to the bile.

The operation of cholecystectomy accomplishes two objects: (1) it removes the local focus of infection when that is present, and (2) it removes the reservoir of bile with its contained stones and stagnated bile. The latter removes a part of the end-product of the pathological disturbance in the cholesterol metabolism which has already taken place; the former removes an agent which has complicated this biological disturbance or which has initiated the stone formation. The only permanent effect accomplished is the removal of the infectious process whenever that is present. The effect upon the cholesterol metabolism *per se* is *nil*. The variations which have been seen in the cholesterol content of the blood after cholecystectomy and their proper interpretation may be summarized as follows:

1. In uncomplicated cases the figures do not change appreciably and the variations are within the normal range.
2. When obstruction is present before operation the complete removal of this is followed by a fall from the preoperative hypercholesterinemia, the figures reaching a normal level very promptly.
3. If the preoperative figure has been low because of an associated high temperature the drop of temperature following operation is accompanied by a rise in the cholesterol content of the blood to the normal level.
4. When the postoperative drop has been large and there had been no antecedent obstruction the fall is due to a lipid-free diet.

The operation of cholecystostomy accomplishes the following objects:

1. It enables one to remove the end-products of disturbed cholesterol metabolism somewhat better than a cholecystectomy without drainage.
2. It affords a surgical method, inferior to cholecystectomy, for draining the infected area. This does not guarantee that the source of infection has been removed and healing may take place before this source has completely disappeared. Recrudescences of infection may therefore be expected and do actually occur. However, there may be occasions when cholecystostomy would yield greater advantage both immediately and perhaps remotely, and when it is certain that no surgical contra-indication exists, such as a strictured or obliterated cystic duct, the procedure should be carried out in preference to cholecystectomy.¹

¹ It may not be possible to determine this accurately at operation without mobilizing the entire gall-bladder and cystic duct. In any case it depends upon individual judgment.

3. It affords a method of biliary drainage. The competence of this method has been discussed in the earlier part of this paper and the method has been compared with common-duct drainage. The effect of both of these methods of drainage on the metabolic activities was also then discussed.

It becomes increasingly evident, now, that a choice of the proper operation, efficiently carried out, combined with the intelligent use of bile drainage, will restore the individual patient to that condition of life and health when no hypercholesterinemic crisis had yet occurred and when no bacterial infection of the bile passages had yet taken place. It becomes evident, too, that the cause of the hypercholesterinemia has been influenced in no way. More particularly it becomes apparent from this discussion that when the primary factor at fault is infection the better operation is cholecystectomy; that when the primary factor at fault is a disturbance in the cholesterol metabolism the essential thing to accomplish is an adequate and prolonged bile drainage in order to deplete the body of the supersaturation of cholesterol; that when, as happens frequently, both of these causative factors are working hand in hand, both of these factors must be remedied by making use of both of the methods of treatment indicated herewith.

Lastly, from the scientific point of view, it becomes evident that when the proper surgical indication is met it becomes immaterial whether a cholecystectomy or cholecystostomy is done, provided the indications of disturbed metabolism furnished by these blood estimations are met by a prolonged and complete bile drainage.

WAR MEDICINE

CONTRIBUTORS

- LIEUTENANT-COLONEL SIMON FLEXNER, M.C., U.S.A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U.S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- MAJOR RICHARD M. PEARCE, M.C.N.A., National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, U.S.N.A.
- MAJOR R. M. YERKES, Sanitary Corps, U.S.A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- MAJOR E. E. SOUTHWARD, Director of Psychopathic Department, Boston State Hospital.
- COLONEL WARFIELD T. LONGCOPE, U.S.N.A. (Prof. Practice of Medicine, Columbia University).
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- COLONEL FREDERICK F. RUSSELL, M.C., U.S.A.
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- MAJOR A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- MAJOR O. H. PERRY PEPPER, M.C., U.S.A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Professor of Pediatrics, University of California).
- MAJOR FRED H. ALBEE, M.C., Director of Military Reconstruction Hospital No. 3, U.S.A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.C., U.S.A.
- MAJOR JOHN A. HARTWELL, Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- CAPTAIN RALPH PEMBERTON, M.C., U.S.A.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

REINFECTION WITH STREPTOCOCCUS HEMOLYTICUS IN LOBAR PNEUMONIA, MEASLES AND SCARLET FEVER AND ITS PREVENTION.

BY LOGAN CLENDENING, M.D.;

KANSAS CITY, MO.,

MAJOR, M. C., U. S. A., CHIEF OF THE MEDICAL SERVICE, BASE HOSPITAL NO. 1,
FORT SAM HOUSTON, TEXAS.

COLE and MacCallum¹ have reported the results of their study of the bronchopneumonia following measles and certain features of lobar pneumonia reinfection, their work having been conducted in the wards of the Base Hospital, Fort Sam Houston, Texas, the hospital in which I have been working. Their report does not concern itself with the incidence of bronchopneumonia in the whole number

¹ Jour. Am. Med. Assn., No. 16, lxx, 1146.

of measles cases, with many types of reinfection in measles other than bronchopneumonia, with pneumonia following scarlet fever, nor with certain features of reinfection in lobar pneumonia. Nor do they make any recommendations concerning prevention.

As a supplementary report to theirs I purpose to give the incidence of *Streptococcus hemolyticus* reinfection in lobar pneumonia, measles and scarlet fever as it occurred at the Base Hospital, Fort Sam Houston; to record the mortality of those various conditions, to discuss, largely by means of case histories, their clinical features and to consider methods of prevention in the future. It will be impossible to do so without using very generously the material collected by Cole and MacCallum.

Reports from various army camp hospitals have indicated that there has been a quite universal experience with *Streptococcus hemolyticus* infection during the past winter. Irons and Marine² have reported it from Camp Custer, Michigan, and Hamburger and Mayers,³ from Camp Zachary Taylor, Kentucky. Irons and Marine's report particularly concerns measles reinfection and Hamburger and Mayer's lobar pneumonia reinfection.

LOBAR PNEUMONIA. From December 1, 1917, to March 1, 1918, there were admitted 319 cases of primary lobar pneumonia; 44, or about 14 per cent. of these, became reinfected with *Streptococcus hemolyticus*. This does not include a certain very small group of cases in which there was a primary streptococcus infection, affecting particularly the chest. These cases of pneumonia were all originally pneumococcus infections, proved either by sputum cultures, blood cultures, lung puncture or tissue culture at autopsy. Clinically, they looked and acted like lobar pneumonia up to a certain point in the progress of the disease. Hamburger and Mayers seem inclined to the view that many of their cases were primary streptococcus septicemias. We have had very few such cases, and I am sure that our cases were primarily pneumococcus lobar pneumonias and that there is a different explanation for the presence of the *Streptococcus hemolyticus*. In fact, in one of our cases an endocarditic vegetation gave a pure culture of Type I pneumococcus and the lung tissue gave a pure culture of *Streptococcus hemolyticus*. Our experience with generalized streptococcus infections was of a different character. Either they followed measles, as Irons and Marine describe, or they were of a much milder character.

The streptococcus infection, then, was grafted upon a lobar pneumonia. In every one of the 44 cases above, bacteriological and clinical evidence, in certain cases, autopsy evidence showed this. The pneumonia epidemic, of which they were a part, was also clinically and bacteriologically a pneumococcus lobar pneumonia epidemic. The streptococcus infection often made itself evident

² Jour. Am. Med. Assn., No. 10, lxx, 677.

³ Ibid., No. 13, lxx, 915.

within a very short time. Often a pleural exudate containing streptococci occurred within twenty-four to forty-eight hours after the entrance to the hospital. But in every one of these cases there was an antecedent consolidation, with pneumococci of a type other than Type IV (which might be a normal finding in the mouth) isolated from the sputum or from the blood. I am not here referring to respiratory or thoracic infection following measles, reference to which is made below.

The clinical complications of these cases fell into four general classes: (1) empyema, (2) delayed resolution, (3) lung abscess and (4) localized areas of persistent pulmonary infection.

1. *Empyema*. Empyema was by far the most common of the complications. The following table shows all the empyema complications of the series of 319 lobar pneumonias, with their bacteriology and results:

EMPYEMA.		Total.	Died.
Fluid showed pneumococcus		22	5
Fluid showed streptococcus hemolyticus		33	17
Fluid showed streptococcus and pneumococcus		1	1
Fluid sterile or undetermined		41	9
Total		97	32

The high incidence and high mortality of the streptococcus infections is at once evident. Over 60 per cent. of the deaths were due to the streptococcus. Add to this the fact that a large number of the cases in Class 4, of undetermined or sterile fluids, undoubtedly were streptococcus and the percentage would go higher. It is interesting to note that the number of pneumococcus empyemata (22) is approximately 6 per cent., a very little higher than the percentage usually reckoned as the average for empyema heretofore in general practice. Lord⁴ found 3.8 per cent. in 500 cases.

The clinical features of our cases were similar to those reported by Hamburger and Mayers. The incidence of empyema with us is lower, but can be explained by the fact that they have reported their measles-pneumonia empyemas along with their primary pneumonias. Our series of measles-pneumonia (*vide infra*) showed nearly 90 per cent. having empyema.

Considering the streptococcus empyema alone it was remarkable how frequently the fluid accumulated early in the disease. The fluid was usually far lower in cellular content than the ordinary creamy empyema pus. It was thin, more or less cloudy, brownish and dirty looking. It was not often present in large amounts but was pocketed and quite difficult to discover in many cases. The difficulty of diagnosis and interpretation of physical signs has been mentioned by all observers. The value of the roentgen rays in

⁴ Diseases of the Bronchi, Lungs and Pleura.

diagnosis, provided proper interpretation is given the roentgenogram, is very decided.

The cases did not do well either with or without operation. We tried early operation, late operation, aspiration and let-alone policy, with about the same results all through. The cause of death was sepsis in every instance. In many cases we had a positive blood culture. When the cases came to autopsy early there would be found an active or resolving lobar pneumonia in one or more lobes, with patches of interstitial bronchopneumonia scattered throughout usually more than one lobe, both superimposed on the pneumococcus process and in clear lobes, and some combination of pericardial and pleural exudates and peribronchial lymphadenitis. The cases which came to autopsy late after operation showed a very extensive and peculiar process of grayish infiltration throughout the lungs, usually grouped as a cortex about the visceral edge of the pleural cavity. These areas invariably showed hemolytic streptococci. They looked like coalescent multiple alveolar abscesses which had not broken down.

2. *Delayed Resolution.* The second group of cases showed the clinical picture of delayed resolution and comprised 6 cases, with 4 deaths. Delayed resolution, as a diagnosis, requires some comment. One has to defend himself against the suspicion of unrecognized empyema. It will be noticed that the sentence above states that these cases showed the clinical picture of delayed resolution; that is, they showed a lobar pneumonia in which temperature and signs of consolidation, with crepitation, and expectoration persisted for a longer period than was to be expected. It may be stated quite explicitly that they were neither cases of empyema nor miliary tuberculosis. The sputum in these cases showed hemolytic streptococci. The following case from this group will give perhaps the clearest possible idea of its clinical features:

CASE I.—Male, aged nineteen years. Entered hospital January 8, 1918. No previous history of measles. There was a lobar pneumonia in the lower lobe of both lungs. Type I pneumococci were found in the sputum. Temperature remained up for fourteen days, respiration and pulse keeping pace.

January 24, the temperature for the first time reached normal. The respiration and pulse were still high.

January 25, the following notes were made: "The patient has apparently had a termination by lysis. He is still very sick: thin and emaciated, with flushed cheeks. He is coughing up thin purulent yellow sputum. There is a dulness, with increased vocal fremitus and abundant sharp, loud, crepitant rales over both sides posteriorly. Aspiration on both sides gives a dry tap."

January 25, leukocytes, 30,000.

January 29, roentgen-ray report: "Cloudiness, diffuse over the base both sides. Diaphragm cannot be seen on the left side."

January 30, examination: "Still coughing up abundant purulent sputum. Physical signs still show dulness and crepitation posteriorly, but the process seems to be clearing."

Bacteriological report on sputum: Contains *Streptococcus hemolyticus*; no pneumococcus.

February 1, blood culture: Negative.

February 1, roentgen-ray report: Left side clear, diaphragm, now plainly seen; right side still dark, both lungs present a feathery appearance throughout.

February 6, leukocytes, 21,000.

February 6, sputum: Negative for tubercle bacilli.

Clinical improvement was steady from February 1 to February 12. The process in the lung seemed to be clearing up.

February 12, it is recorded that a physical examination of the lungs showed them to be fairly resonant and with only a few spots of crepitation. The roentgen rays on this date showed a few dark spots. On the evening of February 12 his temperature rose suddenly and his pulse rate went from 120 to 150. He became lethargic, finally comatose and died on February 14.

The autopsy showed fresh endocardial vegetations on the aortic valve, from which were cultured pneumococci. There was no fluid found in the pleural cavities. In the lungs there were spots of thickened tissue usually around the bronchi. Those spots were not pustular. Under the microscope they showed a typical interstitial bronchopneumonic process. Lung culture showed *Streptococcus hemolyticus*.

3. *Lung Abscess.* There was only one case in this group, a lobar pneumonia, with Type I pneumococcus, who began after an interval of eight days after crisis to run a septic temperature, with profuse expectoration of evil-smelling mucilaginous sputum which contained both pneumococci, streptococci and hemolytic streptococci. The roentgen rays showed a diffuse shadow in the right side. Several diagnostic punctures were negative, but at last the needle drew some pus and mucus, along with considerable air, it having entered what felt like a cavity. Operation at this site drained a pus sac, which required entrance through lung tissue and was evidently a lung abscess draining through a bronchus. The patient is making a good recovery.

4. *Localized Area.* There was a final group of cases which can perhaps be explained best by reciting one or two typical clinical histories. There were 4 cases in this group, all mild and all ultimately ending in recovery.

CASE II.—A boy went through a mild lobar pneumonia of short duration. He was well enough to be up and about, but it was noticed that after exertion his temperature chart showed a slight rise. On examination a spot of dulness, over which there were crepitations and increased vocal resonance, was found over the left

posterior lobe, the site of his original pneumonia. His expectoration, which was abundant, showed hemolytic streptococci, although the period of active invasion it had contained Type II pneumococci. The extent of the area of involvement was never bigger than the palm of the hand. It persisted practically without change for seven weeks and then disappeared, quite completely between two weekly examinations.

CASE III.—Another case, probably with the same pathology, occurred in a Sergeant in the Medical Corps who had a Type IV lobar pneumonia in the lower lobe of the left lung. He made a good recovery, returned to duty and thirty-four days after the crisis of his original pneumonia he had a sudden sharp pain in the lower part of his right chest. His temperature rose and for four days he was gravely ill. His sputum, which was profuse and purulent, not streaked with blood, on culture showed hemolytic streptococcus. Physical examination showed fine mixed with coarse rales over the lower part of the chest in front; the roentgen rays showed a shadow here just above the diaphragm on the right side, quite sharply limited and no larger than three fingers of a man's hand. The fever in this case terminated by lysis and the physical signs cleared up entirely as well as the roentgen-ray shadow.

It is of interest to note in Case III the length of time which separated the pneumonia from the secondary disease. The physical signs, and especially the roentgen-ray findings, raised the question of abscess.

The cases in this group of mild but persistent pulmonary infection have been quite puzzling. We have had no autopsy, so are in doubt as to the exact pathology. Certain features of a clinical picture as profuse morning expectoration and patches of rales, suggest bronchiectasis. But the localized area of involvement and the favorable termination are against this view and suggest a persisting interstitial bronchopneumonia.

MEASLES. Between December 1, 1917, and March 1, 1918, there were admitted to the hospital 716 cases of measles. Our statistics are not reliable as to the exact number of complications by streptococcus reinfection in this group, as we have not cultural reports upon all the otitis media, tonsillitis and peritonsillar abscess cases. Many of the cases of otitis media cultured had streptococci present. So also did certain of the tonsillitides, etc. In all there were about 150 cases of otitis. Aside from the ear and throat complications we had 89 cases of bronchopneumonia in this series (12.5 per cent.), 12 cases of articular rheumatism, non-suppurative, 1 case of suppurative arthritis, with general sepsis, and 2 cases of meningitis, with general sepsis. All of these may be ascribed to the *Streptococcus hemolyticus*. The complications known to be due to the *Streptococcus hemolyticus* in measles were 97 (14.8 per cent.), and counting those cases above mentioned of otitis media and

tonsillitis in which we have no bacteriological confirmation, but in which the clinical features were identical with those in which we have, the number of complications was over 35 per cent. of the total number of cases.

1. *Bronchopneumonia*. There were 89 cases of bronchopneumonia, of which 42 died (48 per cent.). In every one of these cases *Streptococcus hemolyticus* was found either in the sputum or in lung-tissue culture. Other organisms (such as the influenza bacillus) were also present, but irregularly. The report of Cole and others upon this group is so complete as to make it unnecessary to do more than summarize briefly the results.

In all the fatal cases fluid was found in the pleural cavity. The fluid always contained streptococci. The physical character of the fluid was similar to the streptococcus cases of empyema following lobar pneumonia, a murky brown, hardly to be designated as pus. In the whole number of bronchopneumonias there were over 80 per cent. of empyemata. Some of these recovered with operations and some with repeated aspirations. I am not able to come to any conclusion as to the best method of treating them.

Besides the bronchopneumonia there were other groups of cases showing a streptococcic origin. These are not mentioned in Cole and MacCallum's report. I record below a series of cases which will give an idea of the varied symptomatology of this group.

CASE IV.—*Measles followed by double otitis media, meningitis, general septicemia and embolic abscesses. Streptococcus hemolyticus found in the blood culture and spinal fluid.*

The patient, a male, aged twenty-five years, entered the hospital December 12, 1917, with a rash over the skin of the chest, neck and face and conjunctivitis and sore-throat. The throat showed a diffuse redness over the pharynx and buccal mucous membrane. Temperature, 101.2 per cent. By December 16 the rash had faded, the temperature was normal and the patient was comfortable.

December 18, he complained of some discomfort in one ear. The temperature was normal. The ear-drums were pronounced normal by the hospital otologist.

December 19, the otologist again saw the patient and reported there was no discernible indication for paracentesis.

December 21, patient was discharged from hospital feeling well, by his own statement, and with a normal temperature for the preceding seven days.

December 22, he had a pain in one ear and consulted a civilian otologist, who performed double paracentesis, with escape of pus from both ears.

December 23, the patient was comfortable, but in the night he became restless and feverish, called his physician, who found he had a temperature of 104°, and removed him to a civilian hospital. The patient did not improve, so that on December 25 I was asked

to see him. His temperature was then 102°, leukocytes, 26,000; both ears draining thick pus.

December 26, he was removed to the Base Hospital at Fort Sam Houston. The next two days he improved slightly, but on December 29 an abscess appeared over the left elbow and another on the left thigh.

December 30, his neck was rigid: lumbar puncture showed a purulent spinal fluid. On smear the spinal fluid showed streptococci and on culture the colonies hemolyzed blood agar. A blood culture taken on December 29 showed similar organisms. Pus from the ear showed a mixed flora, with streptococci present. The patient died on January 3. No autopsy was made.

CASE V.—*Measles, followed after fourteen days by chill, and polyarthritis; suppuration of the right wrist; hemolytic streptococci cultured from the pus from the joint; blood culture positive for hemolytic streptococci.*

January 13, the date of the patient's entry to the hospital, he had a slight temperature. It is also recorded that he had a rash on the chest, abdomen and face, with pharyngitis, Koplik spots and conjunctivitis.

January 28, he had a chill, and a rise in temperature, followed by several other chills, and the next day developed pain in many joints of the body. Only the right wrist remained swollen by February 2. On this date it was incised and free drainage of pus resulted. The pus from the joint showed *Streptococcus hemolyticus*. Blood culture made on January 31 was reported positive for *Streptococcus hemolyticus*. Blood culture on March 16 was negative. After running a mild septic temperature he developed an abscess on the left hip which was incised April 1. The course of his disease was slow but showed progressive betterment. On present date he is still alive, progressing favorably and picking up some of the weight that he had lost. The wrist has healed. The blood culture on April 22 was negative.

CASE VI.—*Measles, followed by polyarthritis and bronchopneumonia of slight extent; arthritis favorably influenced by salicylates; Streptococcus hemolyticus found in the sputum; recovery.*

This patient, a male, aged twenty-four years, entered the hospital on January 24, at which time his measles was well advanced. A culture of his throat showed the presence of *Streptococcus hemolyticus*.

February 5, he had a sudden rise of temperature, and his cough and expectoration, which had been present during his entire stay in the hospital, were increased. Examination of his chest showed no dulness, but a few spots of crepitation scattered throughout the lungs on both sides. This condition progressed favorably, but on February 14 he developed pain and redness around the joints of the elbows, wrists and ankles. None of the joints suppurred, and under salicylates he recovered entirely. The response to the

salicylates was slower than is ordinarily seen in acute articular rheumatism. The chest condition also cleared up, but slowly. *Streptococcus hemolyticus* was found in the purulent sputum, which he coughed up so abundantly.

CASE VII.—*Measles followed by bronchopneumonia; death sixteen days after entry to hospital; autopsy; lung culture showed Streptococcus hemolyticus.*

The patient, aged twenty years, entered the hospital on January 23, 1918. Symptoms: sore-throat, photophobia, fever and chilliness. Physical examination: conjunctivitis; red pharynx; no tonsillitis. Red crescentic papular eruption over the face and body and cough and expectoration. Diagnosis: measles.

January 28 the fever increased and the sputum was more abundant; it was thin, mucopurulent, greenish gray, but not streaked with blood. The patient was very faintly cyanotic. Quotation from the record February 3: "As he lies in bed a faint duskiness is observable in the face. He is of light complexion, with clear white skin, so that this slight cyanosis is more discernible. There is no flush to his cheek; the eyes are clear; there is no rash on the body. Examination of the chest shows no heart beats; heart sounds are muffled; no murmurs. Right lung in front: no dulness; a few scattered areas of crepitation. The inspiration is twice as long as normal and high-pitched. Left lung in front: resonance good; many large moist rales as well as finer ones. Back not examined this date." From this time on the cyanosis deepened daily, suddenly becoming purplish the day before death. The areas of bronchopneumonia also became larger and more numerous. Death occurred on February 8.

Autopsy showed bilateral lobular pneumonia, confluent on the left side and fibrinopurulent pleuritis on the left side behind. In the left lung the lobules were very distinctly marked out and in the upper lobe on the left side the patches of consolidation were confluent, but distinctly composed of grayish patches clustered about the bronchi. Culture of a piece of lung tissue and culture from the pleural exudate showed hemolytic streptococci.

CASE VIII.—*Measles followed by bronchopneumonia after a period of twelve days; Streptococcus hemolyticus in the sputum; recovery by crisis twenty-six days later.*

This case is recorded as a contrast to Case VII. Case VII was a short, fulminating, rapidly fatal case. Case VIII had a twelve-day period between the decline of the measles and the onset of the pneumonia. During the febrile period cough and expectoration were profuse and the sputum was of the same character as described in Case IV. Physical examination of the chest showed no large areas of dulness but spots of crepitation, especially during inspiration. In contrast to Case IV this patient was never cyanotic. No pleural fluid was discovered. I think it is worth noting that the

febrile period terminated suddenly. This has been noticed in three-quarters of the cases of bronchopneumonia following measles which terminated favorably.

SCARLET FEVER. In 134 cases of scarlet fever we have had 7 cases of streptococcus reinfection. Three of these were pneumonias, with 1 death. One of the other cases had fluid in the pleura containing streptococci and recovered by aspiration. The remaining cases of streptococcus reinfections were otitis media. We have been surprised at the mild character of the scarlet fever cases. Compared to the harassing experiences and hideous mortality of measles in an army hospital, scarlet fever, presumably a more serious contagion, has been of very little moment.

PRIMARY STREPTOCOCCUS INFECTIONS. Both the reports of Irons and Marine and Hamburger and Mayers indicate that they have had to do with a large number of primary, usually pneumonic or thoracic, streptococcus infections. We have not seen many of these cases. There have been 2 cases of apparently primary pleural exudate in which the fluid contained this organism and 6 cases of primary bronchopneumonia. They have not been so fatal nor so severe as the secondary infections, 1 death having occurred in the pleural cases and 1 in the pneumonias. It would seem that the original infection, whether measles or lobar pneumonia (to a less extent scarlet fever), gives to this organism a virulence it does not ordinarily have. A. R. Dochez conveyed to me the impression he had that under ordinary circumstances it did not have a very considerable virulence. So far as I have been able to see I am in accord with this view. We have had quite a number of mild cases of bronchitis occurring among the nurses and staff of this hospital in which hemolytic streptococci were isolated from the sputum.

METHOD OF INFECTION AND PREVENTION. The work of Cole and his associates have left us in no doubt that the streptococcus is spread by carriers in the wards. In one series of studies Lieutenant F. G. Blake found that on culturing all the cases in one measles ward on admission there were 11.4 per cent. of the cases having *Streptococcus hemolyticus* in the throat. Two days later, on a general culture of the ward, 38.6 per cent. were positive and a few days later 56.8 per cent. were positive. This was done in wards in which the patients were separated by sheets and the attendants masked. The attendants and nurses in these wards did not usually have *Streptococcus hemolyticus* in their throats; many cultures were taken and only a few positives were obtained. The organism is not, according to competent bacteriologists, a normal inhabitant of the throat. What, then, determines its particular affinity for the lungs of measles and pneumonia cases? That of course we cannot answer, but we can record that the affinity exists. The bronchitis normally accompanying measles acts as a *locus minoris resistentiæ* and as a culture medium for its growth, and apparently the previous

measles has reduced the immunity of the body. It is obvious that the site and the reduced resistance are also present in pneumonia.

The prevention of these reinfections is an immediate question of paramount importance. Certainly, the next draft should be protected from them if possible. Cummings, Spruit and Lynch,⁵ in an interesting article, suggest the use of vaccines. Their work has, however, not been carried far enough to admit of conclusions. We have tried spraying the throats of all measles patients with dichloramine-T, but with no appreciable diminution in the pneumonia incidence. In the meantime, and until sufficient cases can be tabulated, there are other and easily instituted means of prevention at our command.

It is very probable that if these soldiers had acquired measles or lobar pneumonia and had been cared for at home—not in contact with other cases—the mortality would have been much lower and the incidence of complications, at least in the measles cases, very small indeed. It has long been a matter of record in the text-books that bronchopneumonia following measles was particularly likely to be frequent in hospital wards where a large number of cases of measles were treated. In this respect we are repeating the experience of the old preantiseptic days with puerperal fever: if the patient were treated by a midwife at home she remained well; if treated in a hospital she became infected.

The procedure which we have now instituted at this hospital is to segregate every case of pneumonia, every case of measles and every case of scarlet fever for a twenty-four-hour period. During this time a swab culture is made of the throat. When it has been determined by the laboratory whether or not the patient is a streptococcus carrier he is delivered to a proper ward. We have designated streptococcus and non-streptococcus wards for lobar pneumonia, measles and scarlet fever. None has been made for German measles, as our experience has led us to believe that German measles is not subject to streptococcus complications. Prior to the determination of the presence of the streptococcus in the patient's throat he should have individual isolation—if possible in a room or a tent by himself; if not, then in a room with as few other patients as possible, separated from them so far as possible, and with the most rigid prevention of contact, by use of screens or sheets between beds. With an adequate number of single rooms in a receiving ward this could be accomplished there, it being the duty of the receiving officer to see that all cases are properly cultured and reported to the proper ward. In addition to this it may be necessary to culture the non-streptococcus wards at various intervals, probably once or twice a week, as there will be some streptococcus carriers not detected on a single throat swab. Separation of beds by sheets is of course still necessary.

⁵ Jour. Am. Med. Assn., No. 15, lxx.

The incidence of bronchopneumonia in measles by this method is considerably cut down. It would be unfair to record the statistical results we have had since adopting the plan, as the measles has been diminished and the weather mild, but it promises a working basis for procedure in future epidemics. The result of separating streptococcus carriers with lobar pneumonia has entirely done away with streptococcus reinfections, but here too our results are subject to revision with a more extensive and vigorous epidemic.

A MEMORANDUM ON MILK.

BY DOROTHY REED MENDENHALL, M.D.,

CHILDREN'S BUREAU, UNITED STATES DEPARTMENT OF LABOR.

AN interesting contribution to the question of the control of the price of milk for the use of mothers and young children is given in recent English Acts concerning the "priority" use of milk and the so-called "rate-aided" milk.¹

The milk-supply scheme for allowing a prior claim on the available supply of milk for expectant and nursing mothers and for children up to the age of five years came into practice in late winter and was disappointing in its results. The families who most needed milk and who fell into the "priority" class were able to buy only a fractional part of the milk to which they were entitled, because they could not afford to pay for more.

The Milk Order (mothers and children) received from the Ministry of Food in March empowered the local authorities to arrange for the supply of food and milk to the "priority" class and to supply this food and milk free or below cost price. This was followed by a Local Government Board Bulletin approving of the order of the Food Controller and enabling local authorities to recover 50 per cent. of the expenditure incurred from the grant for maternity and child welfare.

The problem now facing local authorities, who are sanctioned in subsidizing "priority" milk, is whether to interpret the order on a generous scale, as a public health measure, or to limit the expenditure to only the most necessitous cases. The question of the decision of what constitutes a necessitous case presents another point difficult of solution. It has been proposed either to regulate the giving of milk below cost according to the income of the family relative to

¹ Rate-aided Milk, *Maternity and Child Welfare*, April, 1918, ii, 135.

the number of children, or according to the amount expended for rent, which would largely obviate personal investigation.

The price of milk in England today is said to be double the pre-war price, though the Government has attempted to put a maximum price on milk, cheese and butter as well as to regulate the sale of these commodities.

The expenditure for "priority" milk in England, either free or below cost, has been made by the Food Controller and the Local Government Board part of the ordinary expense of war. Regret is felt that in the beginning of the war "priority" milk was not kept at the pre-war price and that any deficit was not met by the nation, as in the case of bread.

While our whole country is agitating the subject of the price of milk and schemes for its control, it would seem an opportune moment to consider the possibility of "priority" milk for our mothers and infants as well as the sale of such milk at a pre-war price.

In *The Food Problem*,² a book put out with the approval of Mr. Hoover, the milk supply is given as the most indispensable part of the national diet and the element in production that must first be maintained and guaranteed in equitable distribution in order that the nutrition of the people may be maintained under the stress of war conditions. Although bread is here put second in importance to our milk supply the price of bread is controlled in the United States and the price of milk is not.

The Food Administration, the Department of Agriculture and the Children's Bureau of the Department of Labor³ are united in their effort to make us realize that milk is our most indispensable food. These departments are endeavoring in every way to keep up the production of the dairy herds of the nation and to check the decline in the use of milk that accompanied the rise in price of milk, especially during the last year.

When the three Government services having to do with the production of food, the sale and distribution of food and the protection of maternity, infancy and childhood agree that milk is the article in our diet most vitally affecting the health of our child population, is it not time that national action was taken to ensure the provision of milk for the "priority" class—nursing and expectant mothers and young children?

Several careful studies have been made recently showing the

² Kellogg and Taylor: *The Food Problem*. Macmillan, 1917.

³ Milk: United States Department of Agriculture and United States Food Administration, United States Leaflet No. 11. *The Agriculture Situation for 1918, Part II. Dairying*, United States Department of Agriculture, January, 1918. Milk: *The Indispensable Food for Children*, Children's Bureau, United States Department of Labor.

decline of the use of milk in certain of our large cities.⁴ It is probably true everywhere that the consumption of milk has been curtailed as the price of milk has increased, and that as yet the children over two have suffered more than the children under two. People generally have become imbued with the idea that good cows' milk is a vital necessity for infants; on the other hand, the idea is still prevalent that milk for adults and older children is not really "solid food" but a pleasant drink, interchangeable with tea or coffee. In this crisis we dare not trust solely to the gradual education of the public to the appreciation of the fact that milk is the most valuable article in the national diet, the indispensable food for the growing child as well as for the infant and the expectant and the nursing mother. More direct measures are required.

The children of England today are reported to be suffering from deprivation of nitrogenous and fatty foods in the early months of the war. England has shown us in her recent Milk Order what might have helped to prevent this malnutrition in young children. Are we to neglect this warning?

AMERICAN JOURNAL OF CARE FOR CRIPPLES.

Edited by DOUGLAS C. McMURTRIE. New York, 1917, No. 2,
Vol. V.

THIS issue of the *American Journal for the Care of Cripples* is one of the most interesting which have appeared since the province of this journal was enlarged to include the problems of the disabled soldier. The extent to which interest and investigation in this field have grown in this country is well illustrated by the nature of the articles which constitute the present issue. It may be said that it is somewhat characteristic of the progress in this line that the illustrations in this and other journals of the sort have now passed that phase of development of the subject which illustrates the care of the crippled only by means of pictures of artificial hands grasping pitchforks.

It is seen at once, in glancing over this issue, that those responsible for its production have been digging progressively below the surface and have done their part to lay foundations for the great work ahead of us. So many and varied are the articles which make up this number that it is difficult to particularize regarding them.

⁴ Milk Prices and the Poor Wage-earner: Weekly Bulletin of the Department of Health, City of New York, November 3, 1917, vol. vi. Studies of the Use of Milk by Families having Little Children: (1) Baltimore, (2) Washington, (3) New Orleans. Children's Bureau, United States Department of Labor.

Among the longest and most important from the stand-point of informatory value to workers in this field are: "Reconstructing the War Cripple in Alberta," by Douglas C. McMurtrie; "Repatriation of the Disabled Soldier in Australia," by Hon. Colonel W. Fitzpatrick, C.M.G.; "Vocational Training for the Canadian War Cripple," by Douglas C. McMurtrie.

It is hardly the function of this review to consider in detail the many humanitarian and sociological aspects which form the basis of much written in this field. It is impossible, however, to omit some reference to this phase of the work, and all readers, lay or medical, will value the description given of the work under way in the neighboring province of Alberta. The illustrations of the article are excellent and show, nearly as well as could, a word description, the conditions and nature of the reconstructive efforts. The fact that the men depicted closely resemble our own men adds to the appeal of the article.

A short article of interest, accompanied by four illustrations, is that on the training for war cripples in Paris.

Under "Vocational Training for the Canadian War Cripple" there is presented a live review of many of the fundamental arguments for widespread and organized effort. Because of some ill-founded criticism directed toward the Canadian Commission, appointed for this purpose, it became necessary, in Canada, to appoint a Parliamentary Committee to inquire into the workings of the system, to test the validity of current public criticism and to give the officers of the commission an opportunity to justify the principles on which their work was based.

In the course of this inquiry a great many witnesses were called, and in the recital of their testimony many side-lights are afforded which could not be obtained through simple description of the work. Nearly fifty pages are devoted to questions by the Committee of Inquiry and answers by the witnesses and defendants, which make interesting and profitable reading. Considerable information is adduced as to the purposes of the work and the means of carrying them out, and there are also included specimens of forms and report blanks in use which reflect accurately their scope and detail.

When the problem of reconstruction and the necessity of meeting it presented themselves with insistence before the general public the novelty of the subject took powerful hold of the popular mind, which was at once stimulated to sympathetic interest. As accounts of this work become multiplied, however, it is seen that much of the literature is repetitive and the tendency will undoubtedly exist for many who make but cursory investigation to feel that with a little reading they have well covered the subject.

This will not necessarily follow, however, and when workers in this field are called upon for sustained practical effort much of emotional interest will have to give way to less stimulating but

fundamentally important details. To those workers who will be found active and untiring when the first wave of sympathy has passed the present number of the journal will prove contributory. It is gratifying to observe in the development of the military side of the journal for the care for cripples evidence not only of firm purpose but also of such thorough knowledge, based on investigation, as to ensure results commensurate with the necessity demanding them.

R. P.

PUBLICATIONS OF THE RED CROSS INSTITUTE FOR CRIPPLED AND DISABLED MEN.

Edited by DOUGLAS C. MCMURTRIE. Series I. Issued February
14, 1918. No. 4.

A STATISTICAL CONSIDERATION OF THE NUMBER OF MEN CRIPPLED
IN WAR AND DISABLED IN INDUSTRY. BY I. M. RUBINOW.

THIS contribution is of such striking interest and the subject is of so large importance that it seems worth while to quote at some length a few of the tables presented, together with the considerations on which they are based. The first part of Mr. Rubinow's article is devoted to evidence showing that previous statistics and previous war experiences are of little avail as a basis for present discussion. He states that in the past military statistics dealt chiefly with gross numbers only, so far as wounds were concerned, without much analysis of the types presented. He says that no reliable statistics or even estimates could be found as to the number of cripples created by previous wars, and that, furthermore, the numbers engaged at present and the differing conditions would make any such statistics of doubtful value, even if available. The following table shows the proportion of battle losses in various wars caused by rifle, artillery and other agencies, and is taken from figures prepared by Colonel Hunter, of the American War College at Washington, D. C.

Army.	Rifle.	Artillery.	All other.
Union (1861-1865)	90.1	9.8	.1
Prussian (1870-1871)	91.6	8.4	.6
Japanese (1904-1905)	83.5	13.5	3.0
Russian (1904-1905)	84.5	14.5	1.0

It seems that in the present War, according to a statement of General Petain, of the French Army, the losses from artillery are over 35 per cent. for the French and 45 per cent. for the German. On the other hand there has been a tremendous improvement in military medicine and surgery. This may have, however, the rather paradoxical result of increasing the total number of invalids by preventing fatal consequences to many injuries which in the past, under less skilful ministrations, resulted in death. It is interesting to note in passing that whereas the number of deaths from disease in the Civil War was more

than twice that resulting from wounds, on the other hand during the first two years of the present War the proportion of deaths from disease was only about 7 per cent. of the whole number. Rubinow gives the following table as a fairly reliable estimate of the killed, wounded and invalids based upon a study made by a Copenhagen Society early in 1917, covering the first two years of the war.

IN THOUSANDS.

CENTRAL POWERS:	Died.	Wounded.	Total.	Invalids.
Austria-Hungary	718	1,777	2,495	533
Germany	885	2,116	3,001	635
Bulgaria	25	60	85	18
Turkey	150	350	500	105
	1,778	4,303	6,081	1,291
ALLIED POWERS:				
Belgium	50	110	160	33
France	885	2,115	3,000	634
Great Britain	205	512	717	154
Italy	105	245	350	74
Russia	1,498	3,820	5,318	1,146
Serbia	110	140	250	42
	2,853	6,942	9,795	2,083
Grand total	4,631	11,245	15,876	3,274

Rubinow remarks that, unfortunately, the data of greatest importance, namely, as to the number of invalids, are probably the least trustworthy. They seem to indicate that on an average at least 30 per cent. of the wounded become invalids. Of the total number of wounded in the Union forces of the Civil War, 14.6 per cent. died, of the German forces of the War of 1870-1871, 11 per cent., of the Japanese forces of the War of 1904-1905, 6.6 per cent., and of the Russian forces 3.7 per cent. In the present War the proportion of deaths has been further reduced, as the following table for Germany indicates:

STATISTICS CONCERNING GERMAN WOUNDED.

	Died.	Dismissed from service.	Returned to duty.
August 1914	3.0	12.2	84.8
September 1914	2.7	9.1	88.1
October 1914	2.4	8.7	88.9
November 1914	2.1	10.6	87.3
December 1914	1.7	10.5	87.8
January 1915	1.4	9.9	88.7
February 1915	1.3	10.0	88.6
March 1915	1.6	9.5	88.9
April 1915	1.4	7.4	91.2

Other tables are given, and the writer finally reaches the general conclusion that, given an army of 1,000,000 men operating for a year, some 40,000 may expect to become crippled through injuries to their extremities, requiring placement facilities or vocational reëducation. Following the same line of analysis, with the reservation that caution is necessary in such estimates, the following table is presented, showing the various injuries to be met with under this group.

Amputation of leg	7,100
Amputation of arm	5,800
Amputation of hand	700
Injuries to leg requiring no amputation	9,100
Injuries to arm requiring no amputation	9,500
Injuries to hand requiring partial or no amputation	7,800
	<hr/>
	40,000

The last half of the article is devoted to a consideration of the men disabled in industry, together with statistics relating to crippled children in the German Empire.

R. P.

REVIEWS

TUMORS OF THE NERVOUS ACUSTICUS AND THE SYNDROME OF THE CEREBELLOPONTILE ANGLE. By HARVEY CUSHING, M.D. Pp. 296; illustrated. Philadelphia and London: W. B. Saunders Company.

THIS book represents a study of tumors of the acoustic nerve. Tumors in the cerebellopontile angle are by no means rare and have been frequently discussed, but this is the first time that tumors of the eighth nerve alone have been so clearly analyzed. The author has probably had a larger surgical experience in this line than anyone else, and of course is competent to speak of them. He begins by an historical review of the literature, the first case having been reported as early as 1830. Cushing has had altogether in his Baltimore and Boston clinics 784 cases of brain tumor, in which 468 have been verified either by operation or autopsy. Of these, 134 were lesions in the posterior fossa, 56 of which were extracerebellar, 30 of the latter arising from the eighth nerve. Then follows case reports of the verified 30 cases. In these the neurological, surgical and pathological data are well presented. Comments follow the presentation of each case.

In Chapter V, Cushing discusses the etiology and incidence of these tumors, and states that acoustic tumors apparently arise from embryonic tissue rests in the peripheral end of the nerve, and their growth may possibly be influenced by such elements as trauma, local infection or pregnancy. A very interesting fact is that the average age on admission of the verified cases was 23.2 years, and he points out that when cerebellar symptoms occur in the first two decades an intracerebellar tumor, more often a glioma, may be suspected. Then follows a discussion of the symptomatology. He summarizes these by stating that "it can be gathered that the symptomatic progress of the average acoustic tumor occurs more or less in the following stages: (1) the auditory and labyrinthine manifestations; (2) the occipitofrontal pains, with suboccipital discomforts; (3) the incoördination and instability of cerebellar origin; (4) the evidences of involvement of adjacent cerebral nerves; (5) the indications of an increase in intracranial tension, with a choked disk and its consequences; (6) dysarthria, dysphagia and finally cerebellar crises and respiratory difficulties."

The discussion of the symptomatology of the eighth nerve tumors is excellent, and where there is so much excellence it might perhaps

be inadvisable to criticise. Nevertheless, it might be well to point out that the discussion of the cerebellar symptoms is not up to date. There is mention of cerebellar ataxia, dysmetria and Babinski's cerebellar hemiasynergy, as if all these were distinctive cerebellar symptoms, whereas all of them are the result of asynergy. It would be well if the term ataxia were not used in association with cerebellar asynergy, for from the reviewer's view-point it should be limited only to such motor phenomena in which there is disturbance of sensation.

In discussing unusual symptoms in eighth nerve tumors, he quotes a number of instances in which pain occurred in the distribution of the fifth nerve, and on page 164 he mentions a case reported by the reviewer. He states: "I feel some doubt, moreover, as to the diagnosis, for one would have expected deafness had the lesion originated from the eighth nerve." As a matter of fact the tumor grew from the fifth nerve and there was no mention in the paper that it grew from the eighth.

The best part of the work of course is the surgical. In this Dr. Cushing's mastery has been acknowledged for years. The author gives his technic, which is well illustrated. There is on page 278 a table giving a chart of twenty-nine operative cases in the verified series. It shows the instance of the prolongation of life in the operative cases. The table shows that the case mortality has been 20.7; the operative mortality, based on a number of suboccipital operations, 39 in all, has been 15.4 per cent. These are excellent results, and illustrate better than anything else Dr. Cushing's suburb operative ability.

T. II. W.

NERVE WOUNDS; SYMPTOMATOLOGY OF PERIPHERAL NERVE LESIONS CAUSED BY WAR WOUNDS. By J. TINEL. Authorized translation by FRED. ROTHWELL, B.A. Pp. 307. New York: William Wood & Co.

THE European War, with all its horrors, has nevertheless been of great scientific value to medicine. Of the different branches of medicine there is none which is likely to gain more than neurology, because of the occurrence of a great number of focal lesions. Already a number of books and papers have appeared on shell shock and on various lesions of the nervous system.

Of discussions on the peripheral nerves the best that has appeared so far is that by Tinel, which is here reviewed. This book was published originally in French in 1917 and an excellent translation was immediately made by Rothwell, after which it was revised

and edited by Cecil A. Joll. The original has a preface by Dejerine, in whose clinic most of the work was done.

Altogether 639 cases were investigated. Of these 408 lesions occurred in the upper limb and 231 in the lower. Of the nerves of the upper limb the musculospiral was injured the most, next following the ulnar, median circumflex and musculocutaneous nerves in order, besides various combinations. Of the lower limbs the trunk of the sciatic nerve suffered most, then the external popliteal nerve, internal popliteal, posterior tibial, long saphenous, anterior crural and so on in order. In other words, practically every peripheral nerve, as well as every cranial nerve, has been injured in this war, and abundant opportunities were furnished the authors to study practically the injury of every nerve in the body.

The book begins with a general survey, the first chapter giving a study of nerve lesions produced in wounds, in which there are excellent illustrations of the various types of nerve sections, tearings, pseudoneuromata, compressions, etc. Then comes a study of the processes of degeneration and regeneration, neuromata, histological lesions caused by nerve wounds and a study of dissociated syndromes and partial lesions. Following this are the methods of clinical examination of a nerve. It is evident that of all of the clinical neurological studies there are none which need more painstaking research than the study of the peripheral nerves, and unless one is equipped by temperament to spend hours in the study of a case a peripheral nerve study had better not be made. Specially careful work must be done, as is shown by the illustrations of the sensory disturbances. It is interesting that only a mention is made of the protopathic, epicritic and deep sensibilities, and that Tinel states that of the ordinary cursory examinations made only the pin method is applied. No further mention is made of Head's work. The clinical types and syndromes are then discussed. The syndromes are those of interruption, compression, irritation and regeneration.

It is interesting that our own S. Weir Mitchell, who first described causalgia in the Civil War, is extensively quoted in this connection. Very unusual cases are cited, especially those of dissociated syndromes. There is an interesting chapter on ascending neuritis, and most interesting are the unusual contractures, brought about in slight lesions of peripheral nerves, a subject which is being developed in this war. Then comes the general diagnosis of peripheral nerve lesions and the specific treatments of the individual nerves, and finally their treatment.

In a word, this is an excellent presentation of peripheral nerve injuries, and shows that a great deal of work must have been done. The illustrations are excellent. No better praise can be given to this book than to say that it carries out the worthy traditions of the Charcot Clinic.

T. H. W.

PHYSICAL REMEDIES FOR DISABLED SOLDIERS. By R. FORTESCUE FOX, M.D., Honorary Medical Director of the Red Cross Clinic for Physical Treatment of Disabled Officers. With Chapters by Major R. TAIT MCKENZIE, R.A.M.C., FRANCIS HERMAN-JOHNSON, M.D., and JAMES B. MENNELL, M.A., M.D. Pp. 277; 88 illustrations. New York: William Wood & Co.

A BOOK by so eminent authority as Dr. Fox cannot be other than valuable. The importance of his subject is extremely great and is one that is going to concern the profession in America more and more in the years to come. There will hardly be a community in the whole country that will not have to consider the care of disabled soldiers even long after the discharge from the army hospitals. The establishment of physical clinics will be imperative. Figures published in France show an average reduction in the mass of physical disability of 20 per cent. by properly organized physical clinics, and this has effected an automatic saving to the State in the charge of pensions of nearly two millions sterling per annum.

Dr. Fox's book is essentially a practical one and presents in a convenient form information which is useful in the treatment of soldiers and civilians by heat and cold, in baths, by electricity and radiation, by massage, mechanical apparatus, exercises and medical gymnastics. Major McKenzie's chapter on exercise, giving minute details as to graduation of effort, is especially good. A chapter on the administration of massage, by Dr. Mennell, though short, covers well the indications and results of such treatment in addition to the administration. And Dr. Herman-Johnson, writing on the use of electricity and radiation, describes the advantages and limitations of such aids. Unfortunately the scheme of the book necessitates repetition of text that ought to have been avoided. The many illustrations throughout the volume add materially to its value as a practical guide.

C. N. S.

THE MEDICAL CLINICS OF NORTH AMERICA. Boston Number, January, 1918. Philadelphia and London: W. B. Saunders Company.

IT is but necessary to recount the contributors to this volume to prove its interest. From the clinic of Dr. H. A. Christian appears a review of some interesting heart conditions. Dr. Elliott P. Joslin gives a masterly discussion of two cases of severe diabetes. Dr. W. P. Graves writes of his personal views and experiences regarding ovarian organotherapy, referring in detail to indications for the several preparations on the market. From the clinic of Dr. Fritz B. Talbot is a presentation of cases of eczema in childhood, with a

clear-cut discussion of etiological factors. Dr. Harry A. Barnes gives a careful review of Vincent's angina. Dr. John B. Hawes describes the early diagnosis of pulmonary tuberculosis. Dr. Andrew Watson Sellards discusses amebic dysentery and associated conditions. Dr. John Lovett Morse refers to empyema in children, but unfortunately the subject does not permit of much more than a review of long-established facts and gives little opportunity for careful analysis which the author is so capable of making. The same might be said of Dr. Richard M. Smith's discussion of pyelitis in infancy, which, however, is well written and also has the virtue of being to the point.

These and many more make this number of the *Medical Clinics* of universal interest and do credit to the men of Boston.

C. N. S.

LECTURES ON MEDICINE. A HAND-BOOK FOR NURSES. By CHALMERS WATSON, M.D., F.R.C.P.E., Lecturer on Clinical Medicine, Edinburgh University. Pp. 295. New York: William Wood & Co.

THIS is a valuable book on general medicine for nurses, and would serve as an excellent guide for any lecturer to nurses. Its language is not too technical, yet the subjects are covered fully, particularly from the stand-point of nursing care. Answering those critics who may think that the lectures go to some extent beyond the requirements of a nurse, the author states as his opinion that the efficiency of a nurse bears a direct ratio to the knowledge she possesses of the nature of the disease of her patient and to the principles guiding the physician in its treatment.

One of the most useful chapters is the last, which describes in detail the principles of diet. Many unusual and extremely useful recipes are given, which are appetizing even in their written form.

C. N. S.

BURNS AND THEIR TREATMENT, INCLUDING DERMATITIS FROM HIGH EXPLOSIVES. By J. M. MACLEOD, M.A., M.D., F.R.C.P., Physician for Diseases of the Skin, Charing Cross Hospital, Royal Flying Corps Hospitals.

EVERY now and then there appears a book that is truly worthwhile. Such is this handy little volume on burns. The author in the hospitals of the Royal Flying Corps and in the skin department of Charing Cross had a rich field of material upon which to base conclusions. He takes up in well-chosen detail the classification of

burns, the treatment including that of regional burns and the prevention of complications.

There are chapters on burns from electricity; from lightning; from roentgen rays; from radium and from corrosives. The final chapter describes the various forms of dermatitis and internal symptoms due to the handling of high explosives. It is exceedingly interesting.

C. N. S.

MINOR MALADIES AND THEIR TREATMENT. By LEONARD WILLIAMS, M.D., Physician to the French Hospital. Fourth edition. New York: William Wood & Co.

To physicians in search for the written experiences of others in the treatment of minor maladies this book will be welcome. It is refreshing in its empiricism, admittedly egotistical and with no uncertainty of diction. It gives the treatment and formulæ that have given the author results in the relief of the symptoms of that great group of a practitioner's patients, namely, those suffering from minor maladies.

There are chapters on colds and coughs, on indigestion, on constipation, diarrhea, vomiting and giddiness, on rheumatism, neuralgia and headache, on goutiness and a very interesting chapter on minor glandular insufficiencies. The author feels that though the microbe—the seed—has ruled the past, the future is with the soil, the endocrine glands.

The book does not permit of much criticism, or rather it admits of so much criticism in its empiricism that it forestalls all criticism. It is, however, well worth while, and the fact that this is the fourth edition proves that it has been a help to many.

C. N. S.

PHYSIOLOGICAL CHEMISTRY. By C. J. V. PETTIBONE, PH.D., Assistant Professor of Physiological Chemistry, Medical School, University of Minnesota, Minneapolis. Pp. 328. St. Louis: C. V. Mosby Company.

THE book is essentially elementary in character, and, as the author points out, his aim was to cover the general field of physiological chemistry in such a way as to make students familiar with compounds that are important from a biochemical view-point and with the fundamental processes which go on in the animal body.

Necessarily, therefore, the student is referred to other standard texts for more detailed information. For those who have no need of going deep into the study of the subject this book will be found

about as suitable as could be desired. The first part deals with the theory, while the second part describes the laboratory work. An appendix gives directions for making up quantitative and special reagents. H. D.

SURGICAL CLINICS OF CHICAGO, DECEMBER, 1917. Vol. I, No. 6; Pp. 220; 89 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number maintains the reputation of this very worthy publication. One is impressed by the selection of cases as well as by the names of those presenting them. They vary widely but maintain throughout the interest of the reader, sometimes because of their importance and infrequency, sometimes because of their importance and frequency, and are of special interest to those surgeons who have not the privilege of the abundant material each contributor to this number possesses. For example, Lewis discusses separation of the epiphysis and T-fractures of the lower end of the femur, myositis ossificans and (with a special discussion on blastomycosis by that authority on the subject, Montgomery) blastomycosis and sporotrichosis. Of special interest are the reports on cancer of the rectum presented by Ochsner, Davis and Bevan. Fourteen surgeons contribute, some on several conditions and all clearly, interestingly and briefly. T. T. T.

INJURIES OF THE FACE AND JAW. By P. MARTINIER, Professor to the Dental School of Paris, and G. LEMERLE, Professor to the Dental School of Paris. Translated by H. LAWSON WHALE, Captain, No. 83, General Hospital, B. E. F. Pp. 345; 168 illustrations. New York: William Wood & Co.

IT is fitting that special attention be given in these days to the repair of injuries of the face and their resulting deformities. The same interest could not have been aroused in surgeons before the war, but most of those now entering the country's service turn to authoritative special treatises on this subject because of their previous unavoidable lack of experience and training. The average physician and surgeon will be first impressed by the amount of work which had been done along these lines even before this war, in which trench-fighting has produced so many and such frightful face injuries. The best work has been done and chief advances have been made by the dental surgeons, who are therefore best qualified to give instruction. This small volume gives most attention to prosthesis or the art of making artificial substitutes for an organ cut off,

two-thirds of it being devoted to this branch of the subject. Although not intended as a technical treatise the methods of treatment and devices which have gained most recognition are explained and largely illustrated. These include the various artificial substitutes for the jaws, larynx, tongue, nose, ears and lips; those which remain exposed to the air and those which remain buried in the tissues. Special chapters are given to fractures of the lower jaw and of the upper jaw, in which is emphasized especially the insufficiency of bandages and slings alone and the value of Cl. Martin's methods of reduction, with troughs sealed by cement, to immobilize when reduction has been accomplished. T. T. T.

RECOLLECTIONS OF A NEW YORK SURGEON. By ARPAD G. GERSTER, M.D. Pp. 347; 20 illustrations. New York: Paul B. Hoeber.

IN this volume of reminiscences the author follows the main incidents of his life from early childhood in Hungary to the time of his recent retirement from active professional life in New York City. He was born in the little city of Kassa, at the foot of the Carpathians, and he depicts graphically the domestic, educational and political environment in which his first years were passed. Later he studied medicine in Vienna in 1866 to 1872 under Hyrtl and Bruecke, Rokitsansky, Skoda and Billroth, when surgical mortality was still appalling. In February, 1873, he first saw a demonstration of the application of the new Listerian method of wound treatment. This was in Volkmann's Clinic at Halle, when the author was on his journey to the United States. First impressions of medical practice in Brooklyn and New York are interestingly described. The opinions he formed of medical students in 1874, and again years later when he took up new teaching duties at the College of Physicians and Surgeons in 1910, are of special interest. This volume of recollections of a busy life will appeal not only to the author's immediate friends and associates but also to a wider circle of readers. W. H. F. A.

MEDICAL RESEARCH AND HUMAN WELFARE. By W. W. KEEN, M.D., Emeritus Professor of Surgery, Jefferson Medical College, Philadelphia. Pp. 160. Boston and New York: Houghton, Mifflin Company.

PERMEATED with the virile enthusiasm of the author, this little book gives us vivid glimpses of the great advances in medicine,

made within the memory of Dr. Keen, now in his fifty-eighth professional year. Interesting references to events occurring when he was a student in Paris or in Virchow's laboratory or to Civil War experiences serve to give one a personal relationship to the events described. The book represents the Colver Lectures of Brown University for 1917, delivered to a general university audience. This mode of presentation demanded a broad, not deep, treatment of the subject, but it has served only to make the book more widely readable and none the less stimulating. It should appeal especially to students of medicine.

W. H. F. A.

INFECTION AND RESISTANCE. By HANS ZINSSER, Professor of Bacteriology, College of Physicians and Surgeons, Columbia University; Major, M. R. C., U. S. Army. Second edition. Pp. 585. New York: Macmillan & Co., 1918.

It was self-evident to those who were familiar with the first edition of Zinsser's *Infection and Resistance* that, with the rapid advancement in the field which it covered and from the excellence of the book itself, a second edition would soon be demanded. In its original form Zinsser's treatise was the first really successful attempt to group and correlate the large mass of important observations and theories that have been collected under the heading of immunology. Previous attempts in English were very inadequate and sketchy, and in no instance compiled by one who had an authoritative and first-hand knowledge of the subject. The extensive monographs in German and French on limited areas of the field, although bibliographically complete, were in most instances of less value from their bias in favor of one or another school of this new science with which their author happened to be identified. An admirable attempt had been made by Emery, some years ago, to give us an outline of the principles of immunity, but his work was rapidly outgrown by increasing knowledge and was also biased in favor of the opsonic school of Wright. There are now several hand-books and laboratory manuals of greater or less excellence in English, some of them elaborately illustrated and most of them accurate in the matter of the experimental details which are used by the laboratory worker in this field. It should be remarked, however, that the advanced worker in bacteriology, who in reality is the only one competent to undertake the practical application of the principles of immunity in diagnosis and therapy, is usually trained in the methods himself and has little need of detailed descriptions of technic, except as he consults them in original articles. It is difficult to see of what value elaborate descriptions of technic can

be to the practising physician who makes constant use of these methods, although he never himself does or should attempt to carry them out with his limited time and experience. What we have all needed, however, both the laboratory worker and the clinician, is a clear-headed, well-balanced discussion of the historical development and present status of the principles of infection and resistance. This is what Zinsser's book has furnished and continues to furnish us with unabated vigor and authority in the second edition. The author himself is an experienced and well-known worker in this field, a contributor as well as a lecturer and applier of the principles which he discusses. Zinsser's presentation of the facts is uniformly marked by a fairness even toward his opponents in those fields with which he is personally familiar. He is among the first in this country to have appreciated the importance of the contributions of the French school of immunity, particularly as exemplified by Bordet, and has never been carried away by the specious argumentation of Ehrlich, as have so many whose knowledge of this field is literary rather than experimental.

The second edition, although keeping in most parts the outline of the first, has benefited and made use of recent advances in the field of immunology. This is notably true in the chapters on anaphylaxis and in those dealing with the practical results of therapeutic immunization in man, where the most recent contributions have been fitted into their proper places and the general summary in each subject thereby to some extent revised. A section on immunity in syphilis has been added and the Abderhalden reaction has been relegated to its proper and less conspicuous place in the general system. The references throughout the book are plentiful and conveniently placed at the foot of the page, and sufficiently ample to lead one to the original sources of information if he so desires. It would be difficult to speak too highly of the scholarly method of this book, its background of first-hand knowledge and its suggestive value in matters of debate, or to overestimate its worth, both to the beginner and the more experienced worker, in this complex and rapidly growing field of medicine. It is a book that should be in the library of every practitioner as well as of every laboratory worker, and it is one which should not be allowed to gather dust on the shelves of him who ministers intelligently to the sick.

F. P. G.

PROGRESS OF MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Bile Peritonitis without Evident Perforation of the Biliary Tract.—BUCHANAN (*Surg., Gynec. and Obst.*, 1918, xxvi, 303) says that effusion of bile into the peritoneal cavity has received serious attention only within the last seven years. He reports a typical case, and the results of a study of the literature, from which he concludes that there is no typical disease picture to account for a bile peritonitis without evident perforation of the bile tract. There is a group of recorded cases, with abundant effusion, in which no perforation could be demonstrated at operation or autopsy. These cases may be accounted for in a variety of ways, some fitting one hypothesis and some another, no one theory suiting all cases. The bilious nature of the effusion still lacks the proof of a chemical examination. It is to be hoped that subsequent cases may be subjected to the test for bile acids and bile salts. The cases being so unusual and so atypical the diagnosis has not yet been made even tentatively, the real condition having never been even suspected in any of the published cases. The treatment should be dry mopping of the peritoneal cavity and direct drainage of the common duct.

The Method of New Joint Formation in Arthroplasty.—PHEMISTER and MILLER (*Surg., Gynec. and Obst.*, 1918, xxvi, 406) made an extensive experimental study on dogs and performed three types of operation, the no-flap, pedunculated and free flap, the results being studied and compared. (1) In the no-flap operations: A joint cavity forms which is diminished in size because of more or less obliteration of the recesses about the margins from thickening and ossification of the capsule and adhesions of the synovia. Excised portions of the capsule and synovia are rapidly but atypically restored. Villous synovitis is frequently present even in the oldest experiments. Articular surfaces form on the ends of the bones as follows: over the prominent

portions which contact with and are pressed upon by the opposing bone, a dense bare bony surface forms which as a result of motion soon becomes smooth and shiny; over the sides, grooves and depressed portions, which are subjected to little or no pressure, a fibrous covering forms by outgrowth from the open cancellous spaces along the surface. With increasing age the fibrous covering usually tends to spread over the entire bony surface, gradually absorbing and replacing the dense bare bony areas. This change is a slow one and in some of the oldest and best functioning joints large bony surfaces were present, the process seeming to be at a standstill. The range of motion varies from 50 degrees to almost normal, and generally was greater in the elbow than in the knee. (2) In the pedunculated-flap operations: The flap early undergoes pressure necrosis and disappears except about the margins and along the grooves where it is not pressed upon. As motion is reestablished, more of the remaining portions are destroyed until eventually little of the flap is left. Only a small part of the base of the flap receives its nutrition through the pedicle. Any other portions which survive become attached to the ends of the bones and participate in the formation of a fibrous articular covering for the region. The changes in the articular surfaces of the ends of the bones are practically identical with those occurring in the no-flap operations. In the regions subjected to pressure a dense polished bony articular surface forms, while in those subjected to little or no pressure a fibrous covering forms partly by outgrowth from the underlying bony surface and partly from surviving remnants of the flap. The size and appearance of the reformed joint cavity and the range of motion were about the same as in the no-flap experiments. (3) In the free-flap operations: The flaps break down and disappear in the same manner and to about the same extent as in the pedunculated flap operations. The changes in the articular surfaces of the bones and the character and mobility of the reconstructed joint are the same as in the other two sets of experiments. Infection, prolonged immobilization, displacement and too extensive and imperfect resection unfavorably influenced all three groups of experiments to about the same degree. *Hence it matters little in experiments on the normal knee and elbow-joints of dogs whether arthroplasty is performed by the no-flap, pedunculated flap or free-flap method. The flaps when used very largely break down and the newly formed joint is about the same, both structurally and functionally, following the three types of operations.*

Arthroplasty with the Aid of Animal Membrane.—BAER (*Am. Jour. Orthop. Surg.*, 1918, xvi, 171) furnishes a further contribution on arthroplasty by the interposition of chromicized pigs' bladder. The object in using a chromicized membrane is to obtain a substance which will remain intact for a long enough period to allow the changes to occur which take place in the construction of the fibrous tissue over the ends of the bones. At the end of the time it should be absorbed, leaving no foreign body, living or dead, within the joint. In this way the joint can approach in character nearest the normal. Such a membrane is found in the chromicized pig's bladder, which has been found experimentally and at second operations on the human subject to remain intact from sixty to one hundred days, a period long enough

to allow a new joint to be made. The greatest possible care in technic is necessary, although there is not the same amount of traumatism or interference with the circulation in the periarticular tissue as is caused by the various flap operations. At the same time the utmost care must be taken in the antiseptic treatment. The author believes that a membrane arthroplasty is the last form of arthroplasty, as no foreign substance remains within the joint. Therefore there is no pain from any remaining interposed living tissue. The operation itself is less extensive than a flap or muscle implantation, and the periarticular tissues are less interfered with. There is no interference with the integrity of a normal part by the removal for a flap of any adjacent structures. Less resection has to be made in order to interpose the intermediary substance. In properly selected cases good, serviceable, painless motion can be obtained by a membrane arthroplasty in most joints, particularly in the jaw and in the hip-joint. In the knee-joints, fibrous ankylosis of the entire joint or bony ankylosis of the femoropatellar articulation gives excellent results by this mode of arthroplasty. In true bony ankylosis of the femorotibial joints the results are still unsatisfactory, but give hope of better results with a better consideration of the difficulties involved.

Fractures of the Skull.—SHARPE (*Med. and Surg. Jour.*, 1918, ii, 319) says that it has become quite a common belief that once a man has had a fracture of the skull and then recovers he is never the same person again. In 1912 he examined the records of three of the large hospitals of New York City during the decade of 1900-1910. The mortality of fractures of the skull was 46 to 48 per cent.; the mortality of the patients operated on was 87 per cent.; this high percentage was due undoubtedly to the operation being postponed until the extreme stages of medullary compression and edema and also to the fact that the operation performed was the "turning down" of a bone flap—a much more formidable procedure than a decompression, and then the bone replaced so that even the benefits of a decompression were prevented. Besides in many cases the dura was not opened, and as the dura is inelastic in adults no adequate relief of the pressure could possibly be obtained. Of the patients, however, who were finally discharged as "well" or "cured" only 34 per cent. could be traced, and of these it was found that 67 per cent. were still suffering from the effects of the injury; that is, two-thirds of them were not as well as before the injury. The chief complaints were persistent headache; a change of personality of the depressed or excitable type, the patient being thus emotionally unstable; early fatigue making any prolonged mental or physical effort impossible, and thus causing inability to work; lapses of memory, spells of dizziness and faintness; and even epileptiform seizures in a small percentage of cases. With few exceptions these cases regained consciousness gradually a few days after the injury and remained in the hospital for periods of four weeks and longer. Their charts made frequent mention of severe headache, a low pulse-rate of 60 or below, signs characteristic of increased intracranial pressure. An ophthalmoscopic examination had rarely been made. Many of these patients still showed the results of the increased intracranial pressure in their fundi and at lumbar puncture. Late decompression gave marked improvement in these cases. The operative findings were always

associated with a "wet," swollen, edematous brain. Sharpe thinks many of the so-called post-traumatic neuroses are superimposed upon this definite organic basis as the result of the brain injury.

The Selection of Abdominal Cases for Operation. — RICHARDS (*British Med. Jour.*, April 27, 1918, p. 471), upon a basis of 200 operations for war injuries, says that the decision as to whether a man wounded in the abdomen should be operated on or not is usually based on the time which has elapsed since the injury and the rate and character of the pulse. Of the patients who survive operation performed in the first twelve hours a high proportion will have had their lives saved by it, and this is true in a lesser degree of those operated on in the second twelve hours. After this time most of those who survive operations are those whose injuries were not originally fatal. Men with a pulse of 120 or over have less than half the chance of survival of men with a lower pulse. Recently wounded men with a rapid pulse should nevertheless be operated on, provided that their condition is as good as it is ever likely to be, that they have a reasonable chance of surviving the actual operation and that the time taken does not prevent the proper treatment of other wounded. Every wound of the abdominal wall, however slight, should be explored, whether signs of internal injury are present or not. If it is found to be penetrating the abdomen should be opened. The necessity for deciding between the claims of abdominal and other cases can be best avoided by good theater organization, the provision of two tables for each surgeon and by not allowing slow operators to do abdominal work. If these measures are insufficient the decision should be left in the hands of the surgeon in charge of the preoperation ward.

A Method of Citrated Blood Transfusion. — ROBERTSON (*British Med. Jour.*, April 27, 1918, p. 477) says that the use of citrated blood for transfusion seems to fill a definite need in that the technic is relatively simple, easily acquired and can be carried out entirely by one medical officer. Furthermore, this method obviates the necessity of having the donor and recipient together, and the blood can be given at the bedside. Stress is laid on the fact that although the technic is apparently simple, certain definite precautions must be observed in the handling of the blood in order to obtain good results. The chief considerations in the technic are to get the blood quickly and cleanly into the citrate, to obtain prompt and thorough mixing of the blood with the citrate and to transfuse the blood so soon as possible after the bleeding. An apparatus is described which can easily be constructed and has been found to work satisfactorily. The blood is received into isotonic sodium citrate, 3.8 per cent. The amount of this solution, 160 c.c., contains 6 grams of sodium citrate, which has no harmful effect. When a good flow is maintained through a needle of adequate caliber and the blood and citrate are well mixed as large a quantity as 800 c.c. of blood may be obtained by this method. A series of 44 citrate transfusions were given under rush conditions at a casualty clearing station, with good results. The immediate effect of the transfused blood and subsequent progress of the cases were fully as good as that seen following ordinary transfusion. No reactions of any consequence were observed.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Two-stage Operation for Carcinoma of the Pregnant Uterus under Paravertebral Anesthesia.—MASON and CONRAD (*Surg., Gynec. and Obst.*, July, 1918) raise the question as to whether it may not be advisable to operate upon pregnant patients having carcinoma in two stages rather than at one time, as is usually done. They describe the following case: The patient, aged twenty-six years, had given birth to one child seven years before, followed by normal recovery. Her previous health had been good. Her last menstruation had occurred about seven months before entering the hospital. She had irregular hemorrhage for three months and pain along the inner surface of the thigh. On examination the patient was poorly nourished, anemic, with hemoglobin index of 55 per cent. The pregnant uterus extended half-way between the umbilicus and ensiform cartilage. On vaginal examination the cervix was hardened, hypertrophied and bled easily upon touch. The patient's condition was so poor that it was thought best no operation should be undertaken; hemorrhage was checked by gauze packing, and the patient was given rest, tonics and forced nourishment until the hemoglobin reached 70 per cent. Sixteen days after entrance to the hospital the patient was given anesthesia by injection from the eighth dorsal to the third lumbar vertebræ and all the sacral segments. The Cesarean operation was performed in sixteen minutes, the abdominal wall remaining relaxed. The baby was ill nourished but cried on delivery, and died six hours later. After the Cesarean operation was completed the cervix was cauterized with the Paquelin cautery and the patient made a good recovery from the operation, but later developed irregular temperature, although the hemoglobin rose to 80 per cent. Twenty-two days after the first operation, under similar anesthesia, the uterus was completely removed. The patient had a very rapid pulse immediately after the operation, but this gradually subsided. In about four weeks after the second operation she left the hospital at her own request. The malignant growth returned and the patient died between four and five months after the first operation. The method of anesthesia employed in this case is of interest: The anesthetic was placed outside the spinal canal about the vertebræ and in close proximity to the nerve trunks as they emerge from the spinal canal through the foramen; each segment is blocked separately, and this is done along the back by using the ribs in the dorsal and transverse processes in the cervical and lumbar regions as guides. A needle the proper length is introduced vertically over the bony landmarks and pushed forward until it meets its resistance; from this fixed point it is not difficult to find the nerve. In the dorsal region the needle is introduced on a level of the spinous process,

about 4 cm. from the medial line, and pushed horizontally inward until the point strikes the rib, then withdrawing the needle nearly to the skin the angle is changed so as to let it pass just underneath the rib and the needle pushed $\frac{1}{2}$ to $\frac{3}{4}$ cm. deeper. Through the point of the needle lying in the intercostal space, 15 c.c. of 0.5 per cent. solution of novocain, with 1 to $\frac{1}{1000}$ adrenalin, is injected. This is repeated on both sides as needed. A somewhat similar proceeding is employed in the sacral region. Before the anesthetic patients are given 10 grains of veronal on the night before the operation and scopolamin and narcophin before the operation. These doses are varied in accordance with the effect desired. Blood-pressure is not much changed and there is little or no depression. The anesthesia continues from two to four hours and then gradually disappears. Patients occasionally have a dry throat which is relieved by taking sips of water.

Blood-pressure in Pregnancy.—DANFORTH (*Am. Jour. Obst.*, June, 1918) gives the result obtained by the study of blood-pressure in 115 private patients and 332 hospital patients. Upon the first series a total of 608 observations were made, the number upon one individual varying from one to seventeen and the age of the patient from twenty-two to forty-three years. The average systolic pressure calculated from the total number of observations is 114, but one patient gave a pressure less than normal, this being 93. There were 24 cases whose ages varied from twenty to forty-three years, and in them the average blood-pressure was 121; the highest pressure was 129. In the hospital cases the pressure reading was done in almost all immediately after delivery. Of those who entered the hospital with pressure below 140 the average pressure on entrance was 119; when the pressure was taken immediately after delivery the average pressure was 116. In all cases when the pressure was 140 or more the history was carefully examined and every effort made by correspondence to find the previous histories of the patient. So far as labor is concerned there is reason to believe that the advent of labor was followed by rise in blood-pressure. From these investigations he concludes that the average blood-pressure of pregnant women is less than that of non-pregnant. In most cases labor causes a rise of arterial tension. The toxemia of pregnancy is accompanied by rise of pressure except in very rare instances, and this rise usually precedes other symptoms.

Two Cases of Extraperitoneal Cesarean Section for Contracted Pelvis.—BROADHEAD (*Am. Jour. Obst.*, 1918) reports two cases of contracted pelvis treated by extraperitoneal section. The first was a negro primipara, aged eighteen years, brought to the hospital in labor. The pelvis was contracted and repeated vaginal examinations had been made. The position and presentation of the fetus was the second with vertex presentation. At operation a suture of plain catgut was passed around the parietal and uterine peritoneum so as to form an enclosed area six inches in length and oblong in outline; incision in the uterus was about five inches long; this was made through the enclosed extraperitoneal layer. After the delivery of the child the uterine cavity was packed with iodoform gauze and the wound sutured with No. 2 chromic catgut. The baby was born in good condition and weighed $9\frac{1}{2}$ pounds. The patient had a high temperature for four

days after operation, then it gradually fell and the patient finally made a good recovery. Eight months later the uterus was suspended or possibly fixed to the abdominal wall. The cervix was closed, firm and high up in the pelvis. The second patient was a primipara who was supposed to have gone over time; to bring on labor an unsuccessful attempt was made to introduce a bag, and a dose of pituitrin was given. The patient was in labor forty-eight hours, having contractions every five to ten minutes, and was examined by five different physicians. On admission to the hospital she was in very poor physical condition; there was feeble uterine contractions and the fetal heart was plainly heard. The extraperitoneal method was chosen because of the many examinations the patient had. Pituitrin was given by hypodermic just before the abdominal wall was incised. As the chorion was opened a foul-smelling, yellowish, purulent fluid escaped freely and was collected for bacteriological examination. The child, a male, weighing $7\frac{5}{8}$ pounds, was delivered without difficulty. Bleeding was moderate, the leukocyte count was 9000 and in spite of the discharge the patient made a good recovery. She was discharged, with the baby, twenty-eight days after her admission. The scar was three inches long, half above and half below the umbilicus. The bacteriological examination of the amniotic fluid showed abundant staphylococci; blood culture done immediately after the operation showed the same germ and some contamination of it. Another case of extraperitoneal Cesarean section was reported by Langrock (*Am. Jour. Obst.*, June, 1918). In his case the indication was contracted pelvis and patient in labor twenty-nine hours before coming to the hospital, during which time she had strong regular pain every five to eight minutes. The membranes ruptured spontaneously at the beginning of labor; the cervix did not dilate. In all the patient had many vaginal examinations. At operation the cut edge of the peritoneum was sutured to the anterior surface of the uterus. One cubic centimeter of pituitrin was given hypodermically and the uterus opened in the midline. The baby and placenta were delivered in the usual way and the bleeding was profuse, but was readily controlled by iodoform packing. The anterior edge of the peritoneum was sutured to the anterior surface of the uterus, leaving an area of the anterior uterine wall exposed. The uterine incision was covered with a continuous suture of plain gut. The final examination of the patient showed the uterus adherent to the anterior abdominal wall over a small area, with the whole of the posterior wall of the uterus, the fundus and a portion of the anterior wall being left to enlarge in a succeeding pregnancy. Mother and child made a good recovery.

Blood Transfusion by the Citrate Method in Bleeding in the Newborn.

—LEWISOHN (*Am. Jour. Obst.*, June, 1918) reports his experience in 9 cases of newborn infants suffering from hemorrhage and treated by transfusion by the citrate method. By this method it is possible to take the blood from the donor at the patient's home and bring the citrated blood to the hospital for use; 100 c.c. is the quantity usually employed. A superficial arm vein in the elbow region of the baby is exposed by a very small incision. The blood is heated to body temperature by warm water and introduced through a fine cannula. As a rule, bleeding stopped immediately and the patient began to gain strength.

Examination of the record of the 8 cases shows two deaths, one in which the patient went to another hospital after examination. In most of the infants the hemorrhage ceased so soon as treatment was begun.

Postpartum Eclampsia.—CASSELBAUM (*Am. Jour. Obst.*, June, 1918) had an opportunity of observing what is comparatively rare, namely, postpartum eclampsia. The patient was aged twenty-four years and the pregnancy in question was her fourth. Four years previously she had had pain over the region of the gall-bladder, was tender and had slight fever. This subsided under rest, liquid diet and ice-bag. A diagnosis of appendicitis and cholecystitis was made, but no operation was undertaken. In the present instance the patient had given birth to a vigorous female child. Two hours after the birth of the child she had a general convulsion lasting two minutes, and up to the time of her reaching the hospital she had four in all. On admission to the hospital the patient was well nourished and well developed, but in a stupor from which she could not be aroused. There was marked jaundice; the pulse was 80; the heart and lungs were negative. There was tenderness in the right upper quadrant from the costal border to three inches below the ribs. A catheterized specimen of the urine showed a large quantity of albumin, casts, blood cells and bile. During the night following admission she had thirty convulsions and was given veratum viride until the pulse reached 60. After this treatment she had five more convulsions. Three days after admission she became rational, had no more convulsions, but was jaundiced and tender over the gall-bladder. Her recovery was complicated by attacks of mental disturbance and finally by a severe pulmonary edema. She made a tedious recovery.

Interstitial Pregnancy.—STONE (*American Journal of Obstetrics*) reports an interesting case of a multipara, five and one-half months pregnant, with symptoms of intra-abdominal hemorrhage. Upon examination the abdomen was distended by a tumor which appeared movable but was strongly inclined to the right side. It was oval in form and unlike a pregnant uterus. As the patient's condition improved, there was slight delay in operating, and when the abdomen was opened there was a free hemorrhage from a rupture in the upper portion of the tumor. Supravaginal hysterectomy was performed, and on examining the specimen it was found that the blood had come from the thin uterine wall. The pregnancy had been interstitial and the growth of the embryo had greatly thinned the uterine wall and lead to hemorrhage.

Emergency Labors.—CHRISTOPHER publishes (*Jour. Am. Med. Assn.*) his notes on 1300 ambulance cases in New York City. Among these there were 19 cases of labor, 14 of incomplete abortion, and 1 of pernicious nausea of pregnancy. No deliveries were made on ambulance calls. Those patients found to be in labor were taken to the hospital as rapidly as possible. In cases in which the ambulance surgeon found the baby born on his arrival the cord was cut and the patient was given the opportunity of going with her baby to the hospital.

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

EMERITUS PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

Summary of Report on Diseases of the Ear, Nose and Throat in Egypt from 1915.—BARRETT (*Jour. Laryngol., Rhinol. and Otol.*, April, 1918) was instrumental in establishing aural clinics at the Australian General Hospital, in conjunction with the ophthalmic clinic, with the result of the extension of this service throughout the British Expeditionary Forces, it being found that the aural work was heavier than the ophthalmic in the beginning, largely on account of the outbreak of measles among the Australian troops soon after landing in Egypt. The number of cases of aural complication of one kind and another as the result of this epidemic, in addition to cases which were a recurrence of a previous suppurative disease of the middle ear, ran into the thousands, there being also a steady inflow of new cases without predisposition, the result of diseases contracted in the immediate service. Of nearly 1500 cases there were 95 of acute inflammation of the middle ear, 435 cases of chronic middle-ear disturbance of catarrhal origin, 139 cases of concussion deafness and 143 cases of otitis externa. There being generally about 100 cases of measles under treatment, a large number of cases of acute inflammation of the middle ear might be expected as a consequence of the measles, but many occurred without apparent association. The severity of these cases was so unusual that pathological examinations were carefully made, but with few exceptions no other organism than the staphylococcus was found. The cases of otitis externa included furunculosis, of which there was a large number, a cause of deafness quite common in the Egyptian service, with an origin not clearly explainable. There were many complaints of impairment of hearing referred to shell shock. A number of these cases were falsifications, but the considerable number which were genuine presented the unusual symptoms of unilateral deafness due to gun-fire. In some cases the membrane was ruptured, but these were not very numerous. Of the bilateral cases of concussion deafness the majority were hysterical, and these made good recovery when placed on rigid treatment and subjected to faradization of the mastoid region. The difficulty of discriminating between the real and the false cases of deafness is much greater than in the cases of blindness. A number of mis-statements were made and a number of devices were resorted to to detect the fraud. Of these the most successful were the bandaging of the eyes and the testing of the hearing at different distances by unknown sources of sound, the man examined being unaware of the distances at which the noise-producing apparatus was placed and giving answers which revealed malingering by their discrepancy. Furthermore, the soldiers were usually unaware of the nature of the Rinné test by the tuning-fork or of the fact that in middle-

ear deafness a tuning-fork placed on the vertex is not infrequently heard best in the damaged ear or in the ear artificially plugged. By these and other devices it was possible to show that in a certain number of cases the degree of hearing possessed did not correspond with the physical appearance of disease and that it varied from minute to minute. But these cases were very few in number and belonged to what the author calls the "pathological residuum of the army." Within a year the aural service in Egypt was well organized and a large number of clinics had been established, aurists were placed in the principal hospitals and, as time progressed, were placed also in the stationary hospitals, in casualty clearing stations and even in the field ambulances. The functions of these aurists in the base hospitals and on the lines of communication were essentially different, the usual practice being to transfer a man to the base who reports sick with ear, nose or throat disease for the first time unless the case is shown on examination to be a trivial one. A case so referred to the base hospital is thoroughly examined and treated and returned to the front, a full clinical report being sent with him. Such a case cannot be sent to the base a second time unless symptoms have redeveloped and without seeing an aurist in the field ambulance or in the lines of communication. Consequently it was the business of the aurist placed on the lines of communication to treat and return to the front all comparatively unimportant cases and to transmit to the base as speedily as possible anything of importance. Statistics show that the aural cases constitute from 60 to 75 per cent. of the total work of the aurist, nasal, pharyngeal and laryngeal diseases constituting 25 to 30 per cent. The purpose of the aural practice being the production and maintenance of efficient soldiers, the problem became one largely of treatment of otitis media and furunculosis, the method of treatment being thorough, daily cleansing of the external auditory canal and middle ear by the patient by means of a cotton stick, the auricle being drawn upward and backward by the finger tips of the opposing hand and the depth of the canal and the middle ear carefully dry-cleansed in the manner mentioned, this cleansing being followed by the instillation of alcohol, with 6 per cent. of carbolic acid lotion; the fluid being allowed to remain in the ear five minutes and the ear again dry-cleansed and stopped with cotton, each case being obliged to report once a week for inspection of the ear. The result of this simple treatment has been gratifying, and is due partly to the fact that the soldier is accustomed to obey orders and therefore carefully followed directions. In reference to shell-shock deafness the author is in doubt as to its existence, having never seen such a case in his experience in the Egyptian service, although other aurists have reported cases in which the impairment of hearing seemed labyrinthine in its origin.

War Injuries and Neuroses of Otological Interest.—From the seven cases here recorded, JONES-PHILLIPSON (*Jour. Laryngol., Rhinol. and Otol.*, April, 1918) concludes that certain parts of the organ of Corti are frequently more seriously damaged than others and that the labyrinth may be rendered hypo- or hyperexcitable, its normal equilibrium being much altered, it being evident also that a greater effect upon the internal ear is produced through an intact drumhead and one

which stands the force of the explosion; and that the effect is less when the membrana tympani lacerates and is still less in the conditions of previous loss of this membrane. In the author's opinion shell-concussion deafness is due to three factors: (1) cerebral concussion; (2) overstrain, and (3) fatigue of the organ of Corti, the former being due to violent oscillations of the perilymph communicated to the organ of Corti and the latter to continuous violent noises or explosions at close quarters. In temporary or permanent disorganization of the conductive apparatus the prognosis depends on the recovery of these parts. In one class of cases the patient experienced a great shock and was in some instances buried by the proximate shell explosion. He became suddenly deaf and also dumb. In some instances also he had paresis of the arm or leg, or both, the higher centers being here involved. Frequently there was an almost sudden improvement in hearing in a few days as the shock passed off and the disappearance of nervous symptoms generally when the patient was removed from the firing line. In another class of cases a portion of deafness remained to be more or less slowly recovered from by the return of the internal ear to a normal or nearly normal condition. In the third class of cases, including structural damage, there is a more or less permanent imperfection of function—a ruptured membrane, a dislocation of the small bones from one another or the stretching of their attachments to the tympanic wall. These are only slowly recovered from in many instances, but the author is able to quote from cases seen three or four months later and showing a considerable recovery of hearing.

Primary Disease of the Labyrinth as the Result of Focal Infection.—SHAMBAUGH (*American Laryngological, Rhinological and Otological Society*, reported in *Laryngoscope*, January, 1918). The clinical phenomena observed in cases of primary involvement of the internal ear as the result of focal infection were quite definite, although the symptoms varied more or less widely in different cases. The defect in hearing was always quite characteristic. It began as a defect in the upper part of the tone scale, while the hearing at the lower part of the tone scale remained even after the defect for the higher notes had become quite extensive. The loss of hearing might consist of a defect more or less circumscribed in the middle of the tone scale. Paracusis willisiana was never a symptom in these cases, and tinnitus aurium was seldom the annoying symptom which it so frequently was in cases of otosclerosis. In most cases both ears became involved sooner or later, the shortening of bone conduction, in such event, being always present. In one-sided involvement the positive Rinne would be changed to a negative in those cases in which the defect in hearing was quite marked. Symptoms arising from the vestibular part of the internal ear constituted a very important part of the clinical phenomena observed in many of these cases. Primary diseases of the internal ear constituted the most frequent cause of vertigo. Primary degeneration of the vestibular nerve occurred quite independently of a similar process involving the cochlear nerve. In these cases an occasional attack of vertigo was the only symptom indicating disease of the labyrinth. Three distinct types of primary degeneration in the labyrinth might be encountered: (1) where the cochlea alone was involved, producing nerve deafness

and more or less tinnitus; (2) where the vestibule was involved simultaneous with the cochlea, producing, as a rule, occasional attacks of vertigo in addition to symptoms arising from disease of the cochlea; (3) where the vestibular nerve alone was affected and where all symptoms indicating disease of the labyrinth might be absent, except for possible occasional attacks of vertigo. The progress of the disease differed widely in different cases. There might be a gradual increasing degeneration of the parts involved; the progress of the degeneration might be accelerated by acute exacerbations; or the acute attacks might be followed by a long period of quiescence. Primary degeneration of the labyrinth was not infrequently a complication of syphilis, hereditary or acquired. It was also observed as a sequel of the infectious fevers, especially mumps, typhoid, measles and scarlet fever. In a large percentage of cases, however, the etiology was not accounted for. It was in these cases that focal infection was suggested as a possible cause. The similarity between the manner in which the labyrinth involvement took place and the involvement of other nerves in which focal infection was known to be the cause, suggested this conclusion.

Concussion Injury of the Ear.—SHUTER (*Jour. Laryngol., Rhinol. and Otol.*, London, February, 1918) states that he has seen a large number of cases on different fronts, and differentiates between machine gunners and concussion deafness; in the former there are more frequently instances of deafness, in the latter a more general lowering of the whole tone scale, they occur more commonly in cases of preëxisting middle-ear disease, and are due not to acoustic concussion but to the pressure waves caused by a shell explosion, as by the explosion of a German mine in a confined space, in trench cases and after proximate bomb explosions, rendering the patient temporarily unconscious and inappreciative of sound for forty-eight hours. These causes are presented for secondary examination, sometimes months after the injury, with the following combination of symptoms, marked decrease in hearing, by bone conduction, tinnitus, paracusis, better aërial hearing in a quiet room and hearing tones of low pitch aërially better in proportion than tones of high pitch.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

Histopathology of Muscle in Gas Gangrene: Contusion, Ischemia and Infection.—RENE SAND (*Ambulance de l'Océan*) discusses the various pathological changes in the structure of muscles in gas gangrene under the three following heads: (1) lesions due to mechanical cause; (2) lesions due to circulatory disturbances; (3) lesions caused by toxic

infection. In his studies he has endeavored to avoid three very common errors, *i. e.*, he did not restrict himself to cases of gas gangrene but made comparative studies, noting the alterations due to direct compression of muscle as well as those due to gas gangrene. In the matter of technic he advises the use of frozen sections rather than those embedded in paraffin, for he believes that in the latter process the muscle suffers a distortion of its fibers, an effacing of transverse striations with a dissociation of myofibrils. His third care was in the matter of cutting out the blocks for study to avoid disfiguring the form and structure of the muscle elements. Of the 50 cases studied the author never found fatty degeneration or infiltration, amyloid or calcareous deposits in the tissues. Of the lesions produced by shock at a distance, contusion, compression or incision, he found the following changes occurred: (1) interstitial hemorrhages, interstitial ecema and edema of the muscle fibers; (2) loss of transverse striations with greater clearness of longitudinal markings; (3) hyperplasia of the nuclei of the sarcolemma; (4) necrosis of muscle fiber. The majority of these alterations are temporary, not found after fourteen days. In the lesions due to circulatory disturbances, total ischemia, ischemia and lymphatic stasis by compression for several hours and prolonged total ischemia with severing of nerve (Volkmann's disease), he observed characteristic changes. At the beginning there was edema of the muscle fibers, with slight interstitial edema, then total necrosis of the muscle and connective tissue and finally the muscle fiber lost all semblance of structure and became a flaky mass. In the third group we find a study of cases of toxic infection in which the characteristic changes are a hyaline degeneration of the connective tissue and muscle fibers and necrosis and fragmentation of the latter. The typical lesions of gas gangrene are hemolysis, hyaline degeneration and necrosis of connective tissue and muscle fibers. It may be that a preliminary contusion is essential for the development of gas gangrene, but the extension of the lesion is the function of the bacillus; where there is no *Bacillus perfringens* there is no gangrene. The microorganism becomes embedded in the interstitial tissue; it fastens itself on the muscle fiber and by its toxins produces degeneration and necrosis of the fiber and penetrates farther only when this fiber is in a state of entire disintegration and death. The action of the toxins of *Bacillus perfringens*, he claims, is incontestable. The reabsorption of the toxic products engendered by the disintegration of muscle brings about certain visceral disturbances, notably nephritis.

Experimental Acute Nephritis.—GOTO (*Jour. Exper. Med.*, 1918, xxvii, 413) supplemented an earlier work on experimental uranium nephritis, with further investigations, using cantharidin, arsenic, diphtheria toxin and potassium chromate subcutaneously in the dog. All animals were carefully controlled for at least two days before the poisons were administered. Albumin and casts appeared promptly in the urine of those dogs receiving cantharidin, arsenic and potassium chromate, whereas their appearance in the urine was delayed for two days when diphtheria toxin was used. Histologically, sections of the kidneys of the different dogs showed varying degrees of congestion of the blood-vessels and convoluted tubules, with granular degeneration of the

epithelium of the convoluted tubules as well as granular plugs in the lumina. In addition, the diphtheria toxin produced shrunken glomeruli and a finely granular material in the capsular spaces. Biochemical determinations were carried out on the blood. The results showed a retention of non-protein and urea nitrogen and chlorides, along with a moderate acidosis. These findings were more marked in the cases of diphtheria and chromate nephritis. The author noted from his experiments, however, that the degree of retention of non-protein and urea nitrogen in the blood varied considerably in different dogs receiving the same dose per kilo of a given poison. A second series of investigations was undertaken to ascertain the effect of sodium bicarbonate upon the course of a milder nephritis produced by the same substances. The sodium bicarbonate was given by stomach tube, for several days, at a constant hour each day. The milder degree of nephritis was gained by giving a smaller dose than was employed in the first series, where almost all the dogs died. It was found that sodium bicarbonate, given in this way, diminishes the acidosis, but that, histologically, the grade of nephritis was apparently unchanged. Little or no effect was noted upon the degree of retention of nitrogen and of chloride in the blood.

The Action of Antiseptics on the Toxin of Bacillus Welchii. In the recent studies on the use of antiseptics it has been shown that they are valuable not only in removing bacteria from contaminated wounds, but also in destroying the toxins of the microorganisms. TAYLOR and AUSTIN (*Jour. Exper. Med.*, 1918, xxvii, 375) carried out a series of experiments upon the toxins of the *Bacillus Welchii*, using pigeons as the indicator for the potency of the toxin-antiseptic mixtures. The toxin was gained by anaerobically growing the microorganisms on special media. The toxin was standardized and then treated with certain antiseptic solutions. The mixture after remaining in contact for five minutes was injected into the pigeon. In this manner it was found that Dakin's solution and chloramine-T will destroy the toxin of *Bacillus Welchii*. The authors believe that similar destruction of the toxin will occur *in vivo*, as was demonstrated by them *in vitro*. Phenol solutions did not exhibit this effect. Pigeons could be protected against multiple lethal doses of the toxin by the addition of the antiseptic solution.

Cultivation Experiments on the Globoid Bodies of Poliomyelitis.—Owing to the technical difficulties offered in the identification of the globoid bodies isolated from cases of poliomyelitis by Flexner and Noguchi, many investigators have been unable to confirm their results. SMILLIE (*Jour. Exper. Med.*, 1918, xxvii, 319), fully cognizant of the problems involved, has undertaken a simpler and more successful method. Poliomyelitis was produced in rhesus or cynomolgus monkeys by virus inoculated intracranially, intranasally or hematogenously. After the disease had reached its height the animals were etherized and small sterile pieces of cerebrum, cord, liver, spleen, kidney or thymus were put into sterile test-tubes into which a sterile piece of rabbit kidney had been placed. About 15 c.c. of sterile, clear, bile-free, relatively fresh, warm, aseptic fluid of no less than 1015 specific gravity were then added. Complete anaerobiosis was obtained by the hydrogen-

nitrogen jar. As many as twenty-five tubes were placed in each jar and incubated for eleven or twelve days. The second generation was made by taking 0.2 c.c. of fluid from the first and subculturing it in other ascitic-kidney media. In addition 0.1 c.c. was planted in tubes containing a semisolid medium. At least five subsequent generations were made. The same criteria as used by Flexner and Noguchi were employed for the determination of the globoid bodies. In all eighteen monkeys were used. In the first 4 vacuum jars were used and the results were unsatisfactory. The material from 3 other monkeys showed streptococci, which the author regarded as agonal invaders. Of the remaining 11, typical globoid bodies were obtained from 7, with a total of twenty-two strains. The largest number of strains per monkey was six; 2 gave only one strain. Nineteen of the completely isolated strains were obtained from the brain, one from the cervical cord and two from the spleen. Eleven completely isolated cultures were encountered. No positive diagnosis was made unless the globoid bodies were found under at least five different fields. Twenty-eight days was the shortest period of time, after the primary inoculation of the media, which was required for a positive diagnosis, while the longest time was fifty-four days. No definitely positive culture was ever found in the first generation. It was found in another series of experiments that the globoid bodies were unable to attack even the simple sugars. Eight different strains which had been isolated by the author were inoculated into healthy monkeys. Three of the animals exhibited some degree of paralysis after intracranial and intraspinal injection. None of the cultivated strains produced typical poliomyelitis. The author concluded from this that very few cultures retain sufficient pathogenicity to cause poliomyelitic infection in monkeys.

Extracts of Antibodies Obtained from Specific Precipitates of Typhoid-antityphoid Serum Complex.—Recently, evidence has been produced to show that large doses of a bactericidal serum administered for therapeutic effect can and often does give rise to "serum sickness." In order to obtain antibodies in a solution as free from foreign protein as possible, WEINSTEIN (*Jour. Immunology*, 1918, iii, 17) precipitated the antibodies from antityphoid serum by a specific antigen, later dissociating the antigen-antibody complex. The agglutinin content of a highly potent antityphoid serum was used as the indicator of a specific antibody. Owing to the resistance of *Bacillus typhosus* to autolysis the method of Chickering in making pneumococcus antigen was found to be unsatisfactory. The author obtained the best results by digesting the bacteria in a 2.5 per cent. solution of antiformin, neutralizing with normal HCl, purifying with absolute alcohol and dissolving in normal saline. Equal quantities of such an antigen and antityphoid serum gave the maximum precipitate, which contained, besides precipitins, agglutinins, complement-fixing, bactericidal and protective bodies. The diluted antigens appeared to be more efficacious than the undiluted. By slightly alkalizing the solution, 5 per cent. of the agglutinins, 50 per cent. of the bactericidal and 60 per cent. of the complement-fixing bodies could be precipitated, whereas strong alkaline solutions promptly destroyed all antibodies. The optimum temperature was 42° C., and there was apparently no advan-

tage in incubating the mixture longer than one hour. Successive washings of the precipitate reduced the agglutinin content. The author was able to confirm the work of Chantemesse and Widal by using simultaneous injections of streptococcus vaccine to increase the virulence of *Bacillus typhosus*. It was learned that 1 c.c. of the anti-typhoid extract would protect guinea-pigs against a fatal dose of typhoid bouillon culture (2 c.c.) and that 0.2 c.c. of the extract would protect mice against 0.2 c.c. of the culture, also a lethal dose.

Typhoid Bacteremia during the Course of Miliary Tuberculosis.—The accurate differential diagnosis between acute miliary tuberculosis and typhoid fever has long been the bane of the clinician. The occurrence of a typhoid bacteriemia in patients dying of miliary tuberculosis is as interesting as it is unusual. BLOOMFIELD (*Am. Rev. of Tuberculosis*, 1918, ii, 28) reports 2 such cases. Both individuals were colored, their ages being eight and twenty-six years respectively. Neither gave a history of typhoid fever. The boy exhibited no clinical evidence of typhoid while the adult showed sufficient signs to be regarded and treated as such. In the youth a pure culture of *Bacillus typhosus* was obtained from the blood stream on the thirteenth and nineteenth days of his illness, whereas the man showed the same organism in his circulatory system only on the tenth day. Both had a negative Widal reaction. The younger individual developed a meningitis, dying in twelve days; the older was operated upon for a perforated duodenal ulcer twenty-four days after his admission and died ten hours subsequently. At autopsy both cases showed an acute miliary tuberculosis. There were no characteristic lesions of typhoid fever to be found in any organ. The author was inclined to regard both as cases of acute miliary tuberculosis, with an accidental bacteriemia of *Bacillus typhosus*. He goes on to say that a one-time carrier state would explain the source of the organisms.

A Rapid Method for the Production of Precipitin Antigen from Bacteria: An Attempt to Apply it to the Determination of the Type of Pneumococcus in Sputum.—KRUMWIEDE and NOBLE (*Jour. Immunology*, 1918, iii, 1) propose a method for the rapid production of an antigen from bacteria by dissolving them in antiformin, boiling, neutralizing, extracting with alcohol, diluting with normal saline, centrifuging and decanting. Emphasis is laid on boiling the suspension in antiformin. Antigens were so prepared from broth cultures of pneumococcus and agar cultures of *Bacillus typhosus*, types of *Bacillus paratyphosus*, *Bacillus diphtheriæ* and *Bacillus mallei*. It was found that unless appropriate dilutions of antigen and sera were employed and the time factor controlled, crossed reactions were numerous and marked, particularly with closely allied organisms. Comparable results, however, were obtained when antigen prepared by the accepted method was used. An attempt to extract a typhoid antigen from the feces was unsuccessful. Antigen was then prepared from pneumonic sputum in accordance with the method above outlined. Equal quantities (0.2 c.c.) of the sputum antigen and type sera were employed and the degree of precipitation recorded. The rapidity of reaction depends, apparently, upon the strength of the antigen. Ordinarily the entire

procedure could be conducted in from one-half to one hour. Positive results were obtained in relatively few cases, although no false reactions were encountered. The authors were impressed by the fact that bacterial antigens are much stronger than serum antigens. They hope to be able to improve the method by future investigations.

Experimental Study of the Pathogenesis of Carcinoma.—YAMAGIWA and ICHIKAWA (*Jour. Can. Res.*, 1918, iii, 1) have undertaken a series of experiments in an attempt to reproduce cancer. Their procedure was to paint a solution of coal-tar upon the surface of the ears of rabbits. By continuing this application over different periods of time, varying grades of epithelial reaction were attained. The authors do not state the exact nature of the coal-tar solution nor the manner of application. Animals were treated every 2 or 3 days for 30 to 360 days. They observed that during the early stages the coal-tar acted as an irritant, inducing a hyperkeratosis. Later, after about 50 days, the hypertrophic epithelium formed elevated and even pedunculated masses. Some of these masses continued to grow after the irritant was withdrawn. As the lesion became still more chronic the epithelial proliferation showed a tendency to downward growth, with invasive qualities. Microscopic examination showed features resembling true carcinomata. They believed that true malignant growth was developed in seven instances, in four of which metastases were found in the regional lymph nodes. The description of the metastases is not clear, and in one case the extension of the new growth is rather assumed than proved. Cancer growth was only obtained in animals which had been treated over a long period of time. In the majority of instances it occurred only after the 150th day. The tissue response to the application of coal-tar differs from the experimental hyperkeratosis induced by means of Sudan III. The coal-tar lesions are primarily pedunculated outgrowths which by the authors are at times spoken of as cutaneous horns. By the procedure of these authors the importance of an irritating agent in the development of new growth is demonstrated.

Acidosis and Acid Excretion in Pneumonia.—PALMER (*Journal of Experimental Medicine*). The study of various urines demonstrates that in the absence of β -hydroxybutyric acid the hydrogen ion concentration and titratable acidity are due largely to the ratio between acid and basic phosphates. Metabolism during the febrile stage of pneumonia results in the production of considerable amounts of acid substances, and the more severe the intoxication the greater the amounts of free organic acid at the hydrogen ion concentration of 5 which are present. There is excreted in the urine of subjects ill with acute lobar pneumonia a large amount of organic acid which is free at a hydrogen ion concentration of 5. The increased ammonia and acid excretion, low carbon dioxide in the blood, diminished affinity of the blood for oxygen and retention of large amounts of alkali indicate an excessive acid production during the febrile stage of the disease. Acidosis as determined by the combined carbon dioxide in the plasma is seldom if ever severe.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,
WASHINGTON, D. C.

A Note on Weil's Disease (Spirochetosis Icterohemorrhagica) as it Occurred in the Army in Flanders.—STOKES and RYLE report the following: Weil first described this disease in 1886. It was characterized by jaundice, pyrexia, hemorrhages and the fact that it was apparently infectious. Epidemics have been known in the United States, India, Africa, Japan and the near East. During the Gallipoli campaign there was a widespread epidemic of jaundice among the soldiers. As to the etiology of the disease, Inada and Ito, in 1914, reported the discovery of a spirochete in the liver of a guinea-pig which had been injected with the blood of a patient suffering from Weil's disease. These authors found later that the blood of patients recovering from Weil's disease contained protective substances against the spirochete they had found. They also showed that when they injected the blood of patients with Weil's disease during the first five days of the disease into the peritoneum of a guinea-pig the animal developed the symptoms of the disease and they were able to show the spirochete in the liver and blood of the animals in large numbers. The experiments made with normal people and patients with catarrhal jaundice showed no such results. These writers state that as the illness progresses the spirochetes disappear from the blood stream and cannot be demonstrated in the tissues. Weil believed that the infection was through the alimentary canal and Inada supports this view. Ito and Oki, however, have been able to communicate the disease to animals by applying infected material to the uninjured skin, and they therefore think it may be communicated to man by the skin being exposed to infective material. Fifteen cases of Weil's disease have come to the notice of the authors and they have been able to confirm the findings of the discoverers of the pathogenic cause of the disease. In 2 cases they have infected the animals which have shown the characteristic pathological changes and from which it has been possible to demonstrate the spirochetes. With the exception of 1 case all the men at the time of the onset of the disease were or recently had been employed in the trenches. Two of the cases proved fatal. The characteristic symptoms are as follows: The patients have generalized pains in the head and lower limbs, complain of weakness and unsteadiness. Most of them say they have been vomiting and some of them have nosebleed. The onset is accompanied by a temperature of 103° F. On admission the most striking symptoms were the jaundice and the extreme injection of the

conjunctivæ accompanied by great prostration. The authors found, in investigating the symptoms in the alimentary system, that the tongue is very dry, brown and fissured, that all the patients were constipated and vomiting in the early stages occurred in every case. The appetite which was lost during the period of pyrexia, returned as soon as the jaundice began to fade. As to the circulatory system, the pulse rate was, as a rule, slow in proportion to the pyrexia and there was a very definite slowing during convalescence. There was no evidence of respiratory complications. The excretory system was not greatly affected, the only change observed being a slight albuminuria during the pyrexial period in all cases. There were no severe nervous symptoms except in the grave cases. All the cases showed enlargement of the glands. Varying degrees of jaundice were seen. It was usually a lemon or orange tint and the color rapidly decreased as convalescence began. All cases showed an irregular pyrexia and subnormal temperature was common in early convalescence. In summarizing their experimental results the authors say that they had only two positive results among the animals injected with the blood of patients and no positive results were obtained after the sixth day. The infected guinea-pigs became ill between the fifth and seventh days. Their temperature rose to 104° F. and typical pathological changes identical with those described by the Japanese workers were demonstrated by a postmortem examination. Spirochetes were demonstrated in the livers in large numbers. In conclusion, the authors state that they believe the cause of epidemic jaundice in Flanders is identical with that described by the Japanese investigators and that the infective possibilities of the disease should be recognized.

The Etiology of Scarlet Fever.—MAIR (*Journal of Pathology and Bacteriology*) gives a preliminary description of the diplococcus scarlatinae which he isolated from the throats of scarlet fever patients in 1915. In the present paper he gives a more complete description of this diplococcus with the technic employed for its isolation and identification. He also presents additional evidence in favor of its causal relationship to the disease. The organism can be demonstrated in the throats of scarlet fever patients during the first week of the disease in 87 per cent. of the cases and it disappears, as a rule, from the throat about the fifth week of convalescence. The diplococcus produces in monkeys a disease which in many respects resembles scarlet fever. It is confined to the region of primary invasion. The most outstanding clinical feature of scarlet fever, namely, the rash, has not been reproduced in monkeys.

Further Attempts to Transmit Pellagra to Monkeys.—EDWARD FRANCIS (*Hyg. Lab. Bull. No. 106*) states that the opinion of some workers that pellagra is a specific infectious disease, and the report by Harris, of New Orleans, of the production of pellagra in the monkey by the injection of a Berkefeld filtrate of pellagrous tissues, led the United States Public Health Service as a part of its study of pellagra to attack exhaustively the problem of the infectivity of pellagrous tissues and body fluids for the rhesus monkey. The experiments here reported consist of a series of inoculations and feedings of pella-

grous tissues and fluids into 90 rhesus monkeys, 3 baboons and 1 Java monkey. The experiments here recorded constitute the most exhaustive effort of its kind ever made to infect monkeys from pellagrous tissues. The experiments were begun at the United States Marine Hospital, Savannah, Ga., in July, 1913; were continued through 1914, and were completed in June, 1915. Throughout this period the experimental animals were bountifully fed and were kept under daily observation in cages in a glass-covered conservatory, located on the south side of the hospital and freely exposed to the direct rays of the sun. The sources of the pellagrous material with which the animals were inoculated or fed were 10 autopsies and 50 living pellagrins. In all, 252 experiments were made with material collected during life or at autopsy; in 141 of these, inoculations were made by hypodermic needle; in 82, material was fed by stomach-tube; in 29, feces were applied to the nasal mucosa. With few exceptions each animal was inoculated by more than one route, with two or more kinds of material, from more than one case, and on more than one occasion. Twenty-eight animals were each subjected to a single experiment; 19 were each subjected to two experiments; 17 were subjected to three experiments each; 19 were subjected to four each; 7 were subjected to five each; and 4 were subjected to six experiments each. The material used for inoculation or feeding was disposed of as follows: (a) The brain, spinal cord and their membranes were removed at 8 autopsies and injected cerebrally, venously, subcutaneously, muscularly, peritoneally or spinally into 29 rhesus monkeys. (b) The buccal, thoracic and abdominal organs except intestines were removed at one autopsy and injected venously or subcutaneously into 10 rhesus monkeys. (c) The intestines and fecal contents were removed at 7 autopsies and injected venously, cerebrally or subcutaneously into 18 rhesus monkeys, 2 baboons and 1 Java monkey. (d) Skin showing the pellagrous lesions was removed at 5 autopsies and injected cerebrally, venously or subcutaneously into 9 rhesus monkeys and 1 Java monkey. (e) Blood drawn from 8 pellagrins was injected venously, spinally, muscularly or peritoneally into 11 rhesus monkeys. (f) Cerebrospinal fluid collected at 5 autopsies was injected cerebrally, venously or spinally into 16 rhesus monkeys. (g) Spinal fluid collected during life from 28 pellagrins was injected immediately after collection, spinally, into 24 rhesus monkeys. (h) Pericardial fluid collected at 1 autopsy was injected venously or spinally into 4 rhesus monkeys. (i) Urine from 4 pellagrins giving a marked indican reaction was injected venously into 5 rhesus monkeys. (j) Feces from 3 pellagrins with marked diarrhea were after Berkefeld filtration injected peritoneally into 26 rhesus monkeys. (k) Feces from 1 autopsy and from 2 living pellagrins were introduced on cotton pledgets into the nasal fossæ of 29 rhesus monkeys. (l) Sputum collected fresh each day from 10 spitting pellagrins was fed by stomach-tube to 5 rhesus monkeys. (m) The brain, spinal cord and their membranes collected at 2 autopsies were fed by stomach-tube to 25 rhesus monkeys and 2 baboons. (n) The entire contents of the buccal and thoracic cavities collected at 2 autopsies were fed by stomach-tube to 16 rhesus monkeys and 3 baboons. (o) The entire contents of the abdominal cavity collected at 4 autopsies was fed by stomach-tube to 17 rhesus monkeys and 3

baboons. (*p*) The entire contents of the buccal, thoracic and abdominal cavities were removed at one autopsy, mixed with spoiled corn meal and fed by stomach-tube to 18 rhesus monkeys and 1 baboon. (*q*) Feces collected at 1 autopsy were mixed with spoiled corn meal and fed by stomach-tube to 2 rhesus monkeys. (*r*) Feces collected fresh each day from a fatal case of pellagra with diarrhea were mixed with spoiled corn meal and fed by stomach-tube daily for fifteen days to 6 rhesus monkeys. *Result:* The animals thus experimented upon showed no indications suggesting pellagra nor did they furnish any support for the view that pellagra is an infectious disease.

The Diagnosis of the Enteric Fevers in Inoculated Individuals by the Agglutinin Reaction.—DREYER and WALKER (*London Lancet*) believe that the agglutinin reaction is the most valuable method of diagnosis for the enteric fevers (typhoid, paratyphoid A and B), as the percentage of positive results obtained by culture methods alone does not exceed 50 per cent. In making the tests for agglutinins after inoculation some accurately quantitative method should be substituted for the qualitative methods formerly practised, diagnosis should depend upon a series of several successive observations and the method employed should produce definite and accurate measurements relative to some fixed standard: for instance, the standard agglutinable cultures prepared at Oxford. These methods would do away with the difficulties which arise from the wide practice of inoculation and would help to disprove the statement that protective inoculation against B. typhosus or the paratyphoid bacilli renders the agglutinin reaction less reliable than it is in non-inoculated individuals. The authors state that on the one hand active infection can be diagnosed as well in typhoid-inoculated individuals as in non-inoculated persons; and, on the other hand, the absence of inoculation agglutinins within the first twelve months or more after inoculation is a very rare occurrence in properly inoculated individuals and is no more frequent in the subjects of pyrexial attacks than in persons who remain in perfect health. The writers then attempt to show that the statements and methods of Dr. H. S. Tidy published in connection with a discussion of paratyphoid fever are erroneous. His method of comparison of the number of standard agglutinin units found in normal inoculated individuals with the number found in inoculated persons suffering from paratyphoid fever or other febrile condition is fallacious. His statement that inoculation agglutinins disappear or are diminished as the result of febrile attacks is shown to be disproved as well as his assertion that a serum titer of 100 standard agglutinin units "apparently corresponds to a positive reaction in non-inoculated persons." He claims also that from tables published by Dreyer and Torrens "it is evident that the febrile cases have distinctly less typhoid agglutinin than the normal inoculated persons," but the authors show that he has misinterpreted the data in these tables and has no true evidence to support this claim. Their contradiction of Tidy's statement that inoculation agglutinins disappear or are diminished as the result of febrile attacks is in perfect agreement with the careful work of Grattan, Harvey and Wood on paratyphoid fever in India. These workers showed that in undoubted cases of paratyphoid A fever in typhoid inoculated individuals a marked

increase in the agglutinins for *B. typhosus* was noted. The question as to whether inoculation agglutinins are diminished after the fourth or fifth day of pyrexia can only be settled by following the serum titer of individuals during the course of an infection by exact quantitative measurements capable of reduction to a constant standard. From the study of a series of cases the writers found that although the typhoid agglutination titer may remain unchanged or only slightly increased during the course of paratyphoid fever, if affected at all, the change produced is one of active rise, either antecedent to or occurring at the same time as the beginning of the rise in paratyphoid *B.* agglutination titer. In diagnosing mild cases of typhoid and paratyphoid in inoculated persons, of which many occur, a quantitative determination of their agglutinin titer for typhoid and paratyphoid bacilli on three or more successive occasions at a few days' interval should be made before the presence of typhoid or paratyphoid infection can be excluded. In the interpretation of the agglutinin curves it is important to note the exact time of the maximum agglutinin titer, which should occur between the sixteenth and twenty-fourth day of the disease. If there is any deviation from this, careful inquiry should be made as to the accuracy of the dates, and the results should be carefully interpreted.

Anopheles Infectivity Experiments.—MITZMAIN (*Public Health Reports*, September 1, 1916, vol. xxxi, No. 35) states that in 17 experiments in which human beings were employed to test the infectibility of *Anopheles punctipennis* with *Plasmodium vivax*, 14 cases of malarial fever resulted. The sporozoites in the mosquitoes used developed ten to twenty-two days after the definite hosts were given an opportunity to bite a patient harboring a scanty number of mature tertian gametocytes. In an attempt to infect several persons with a single specimen of *Anopheles punctipennis* one mosquito proved to be the sole infective agent in 1 experiment and one proved to be the sole infective agent in 3 experiments. These two specimens when applied to the same person transmitted the infection in 5 cases, while one of them used with a third mosquito succeeded in infecting 4 persons. In these experimental inoculations it was demonstrated that in 9 instances in which two mosquitoes succeeded in transmitting malaria at least one of the pair was proved to be capable of causing the disease when used singly. It was demonstrated in 11 experiments that short exposure to bites was sufficient to cause successful transmission of the disease. In all of the successful inoculations only tertian infection was reproduced. *Plasmodium vivax* was demonstrated microscopically.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

NOVEMBER, 1918

ORIGINAL ARTICLES

**A NEW DIAGNOSTIC SIGN OF FOREIGN BODY IN THE
TRACHEA OR BRONCHI, THE "ASTHMATOID
WHEEZE."**¹

By CHEVALIER JACKSON, M.D.,

PROFESSOR OF LARYNGOLOGY, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

It is needless before a meeting of this character to elaborate upon the necessity of developing to the utmost all diagnostic means for use particularly in cases of foreign bodies not opaque to the roentgen ray. It is also unnecessary to do more than allude to the well-known fact that pathological shadows often show the presence of a foreign body that is itself not opaque to the ray. The absence of such shadows, however, we know is not an indication that a foreign body is not present. Auscultation and percussion are, of course, extremely valuable in many cases, though here, also, a negative report is much less valuable than a positive one. It is a great misfortune that in many cases of foreign body of great density, showing clearly in the ray, such as metallic bodies, auscultation and percussion, have been neglected. The writer has endeavored to obtain records as complete as possible in all of his cases, for their statistical value, regardless of whether the ray was positive or negative. To the well-known physical signs he has added a new one which he has called the "asthmatoïd wheeze." He regrets, however, that his statistics on this sign do not go back so far as his other statistics.

¹ Read before the meeting of the American Academy of Ophthalmology and Oto-Laryngology, Pittsburgh, Pa., October 29, 1917.

The presence or absence of the asthmatoïd wheeze has been recorded in 62 cases. From this record the author feels that we have a new sign that promises to be of great value in many cases in which the foreign body is not opaque to the ray. He has called this new sign the asthmatoïd wheeze because the sound is somewhat similar to the wheezing heard when the ear is placed to the open mouth of an asthmatic patient. The chief difference is that there is more or less association of the sounds of rales with the wheezing in asthma, while in the asthmatoïd wheeze of the foreign-body case the sound is drier, when typically elicited, though of course it may be associated with more or less secretion, adding more or less of the sounds of bubbling. In a typical case, however, such as No. Fbdy. 623, the wheeze is much more marked after the coughing out of all secretion than before. This phenomenon is quite likely due to the secretions, more or less completely occluding the spaces by which air escapes between the wall of the bronchus and the irregularly shaped foreign body itself. When these irregular air passages are cleared out more air passes, and consequently the wheezing sound is louder.

The author has deemed it best to call the attention of his confrères to this sign without waiting longer for accumulation of data in order that its value may be determined by the largest number of observations.

Numerous cases are reported in the literature in which audible sounds in foreign-body cases have been studied, as heard with stethoscope or naked ear applied to the chest wall or over the cervical trachea or larynx, but I have been unable to find in the literature any mention of a study of the sounds as emitted from the open mouth. The nearest approach to it is the often mentioned "croupy cough" indicative of a laryngeally lodged foreign body; but even in these cases there is no mention of the study of the respiratory as distinguished from the bechic sounds. It is, however, not in the laryngeal cases that the asthmatoïd wheeze is elicited. It is in the tracheal and bronchial; hence the great importance of the sign. If there is a croupy cough the larynx must be looked at. This is readily done and the matter of laryngeally lodged foreign body is readily decided, positively or negatively; but the indications for bronchoscopy in suspected foreign-body cases are often not so clear, and one feels that the indications in some cases are worthy of more thorough study than in a laryngeal case before a decision to do or not to do a bronchoscopy is reached.

DESCRIPTION. The asthmatoïd wheeze may be defined as a sound heard by placing the ear in front of the patient's mouth during expiration. It resembles the wheezing of the asthmatic patient, but is drier. It is caused by the vibration of the air passing the foreign body in the bronchus. It is elicited by placing the ear in front of the open mouth of the patient while breathing deeply and

regularly in and out. If the wheezing is not noticed the patient is asked to carry respiration to the extreme limit as though endeavoring to expel all of the residual air from the lungs. In a number of instances the wheezing has been apparent only at the termination of this prolonged forced expiration. In many other instances the wheezing was so loud that it was noticed all over the room. In eliciting it care is needed to distinguish between a wheezing caused by secretion and a wheezing caused by a foreign body. This cannot always be done with certainty. Moreover, more or less secretion is usually present in the neighborhood of the foreign body. Usually the sounds of secretion disappear after coughing and expectoration, while the wheeze of a foreign body remains after the most violent and persistent coughing unless the foreign body has shifted.

The pitch and loudness of the sound seem to depend upon the size, position and shape of the foreign body, as on these characters depend the size and shape of the spaces through which the expired air passes the foreign body. In one case the wheeze terminated in a sharp smacking sound, due to the impact of the suddenly arrested foreign body which had been dislodged.

LOCALIZATION. The asthmatoïd wheeze is of no localizing value. Being a sign heard at the open mouth, not with the ear at the chest wall externally, it is impossible to determine out of which bronchus the wheeze comes. In one case a foreign body in the trachea gave a slightly different note, very much flatter in tone, as compared to the note as heard in cases of bronchially lodged foreign bodies. Whether or not further observations will establish this to be the case, and if so whether or not it will be possible to determine by the absolute pitch whether the foreign body is located in the trachea or in a bronchus, it is impossible to say at present. Observation by those having well-trained ears will be very valuable here.

PHYSICAL CHARACTER OF FOREIGN BODIES PRODUCING THE ASTHMATOÏD WHEEZE. Smooth, rounded foreign bodies that cork a bronchus tightly have not, in any instance, produced the asthmatoïd wheeze, properly so called. Many of the cases of cork-like foreign bodies associated with considerable amounts of secretion in the trachea and bronchi have caused a moist wheeze, but this sound is of less diagnostic value. The sound was elicited clearly and sharply in cases of foreign body of larger diameter than a pin, and especially in those of angular shape, such as bones, nut-shells, grains of corn and the like.

MECHANISM OF THE PRODUCTION OF THE ASTHMATOÏD WHEEZE. This is, of course, conjecture. It seems quite probable that the sound is produced by the air passing the foreign body; in other words, by passing through a very much diminished area of cross-section and passing over or impinging upon rough, sharp surfaces instead of passing, as it normally does, through the round, relatively smooth mucosa-covered air passages.

REPORTS OF CASES. To report in detail all of the cases in which the asthmatoïd wheeze was searched for would needlessly prolong this paper. The test was made in 62 cases in all. Of these the wheeze was present in 41 cases of foreign body and absent in 21 cases in which the foreign body was afterward discovered or previously known to be present. The following cases are typical of the classes in which the wheezing was present and absent respectively:

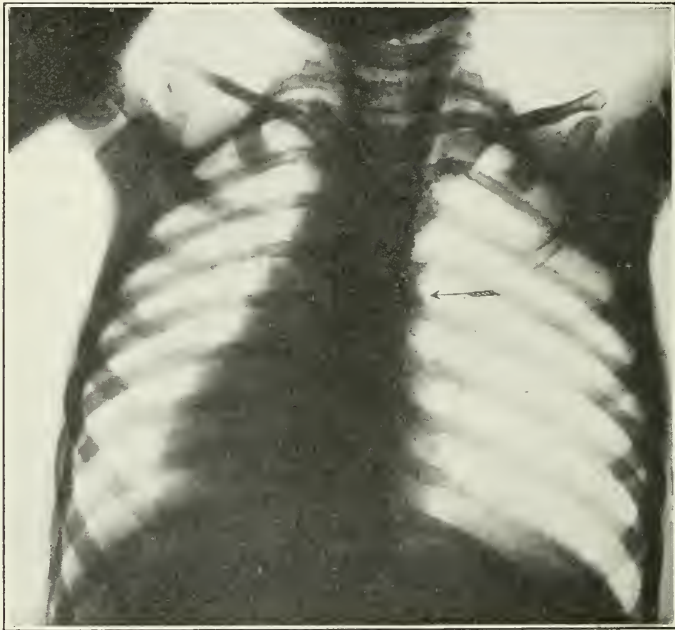


FIG. 1.—Radiograph showing pebble in right bronchus of a child, aged four years. The “asthmatoïd wheeze” was absent in this case, presumably because the pebble (Fig. 2) “corked” the bronchus so completely that no air could pass. (Radiograph made by Drs. Manges and Bowen. Case No. Fbdy. 624.)

CASE No. Fbdy. 624.—*Pebble removed by oral bronchoscopy from right bronchus; asthmatoïd wheeze not present.* J. W., a girl, aged four years, was referred by Dr. O. W. Saunders, of Camden, N. J., for the bronchoscopic removal of a pebble aspirated two days previously. The child had been playing with pebbles, a number of which she had in her mouth. Following the aspiration there were dyspnea, coughing, vomiting and blood-streaked sputum at irregular periods. Dr. Edwin E. Graham reported diminished expansion and harsh breath sounds from the upper right anterior portion of the chest. The radiograph (Fig. 1) made by Drs. Manges and Bowen was reported upon as follows:

"In the case of J. W. there is a remarkable condition in that the foreign body is surely in the right bronchus with the right lung showing completely aerated, whereas the left lung casts a considerably more dense than normal shadow, as if there had been some inflammatory process in the left side. It occurs to me that probably the foreign body was at first lodged in the left bronchus and remained there until a comparatively short time before the roentgen-ray examination was made. After the foreign body was removed there seemed to be less difference in density between the two sides, but still a shade of difference.

"This difference in density of the two sides might, so far as the plate is concerned, be due to overdistention of the right lung with air—in other words, a temporary emphysema. If it were possible that this pebble could have acted as a ball valve, admitting air but not letting it out, the results would accord with the appearance on the plate."



FIG. 2.—Pebble that did not cause an asthmatoïd wheeze presumably because it fitted so tightly in the bronchus. Pebble removed bloodlessly through the mouth by bronchoscopy without anesthesia. (Case No. Fbdy. 624.)

On testing for the asthmatoïd wheeze by putting my ear to the patient's open mouth I was unable to detect any abnormal sound.

Bronchoscopy without anesthesia, general or local, revealed the pebble tightly wedged in the right main bronchus above the upper lobe bronchus, from which it was disimpacted and removed in three minutes fifteen seconds. Recovery was prompt and complete.

Remarks. The absence of the wheeze in this case was doubtless due to the tight, cork-like fitting of the pebble in the bronchus, preventing escape of any air past the foreign body (Fig. 2).

CASE No. Fbdy. 623.—*Bone removed by oral bronchoscopy from right bronchus; asthmatoïd wheeze diagnostic.* Male, aged thirty-nine years, was referred by Dr. Schlindwein, of Erie, with a history that while eating beef soup he had gagged on finding in his mouth a bone which he was unable to extrude. A deep inspiration aspirated the bone. The immediate symptoms were: laryngeal pain, severe coughing, blood-spitting, wheezing, substernal pain and labored respiration. An unsuccessful bronchoscopy had been done before the case reached Dr. Schlindwein, being followed by a temperature elevation to 104° F., severe coughing, foul sputum, increased spitting of blood and dyspnea, with total aphonia. An excellent radiograph (considering the enormous size of the patient's chest) failed to

show any evidence of foreign body. The larynx was not edematous, though lacerated.

Physical examination of the chest by Dr. W. H. Spencer was reported as follows:

"Thorax rounded. Thick walls. Expansion poor, seems equal. Percussion seems clear—slightly impaired generally because of thick chest walls. Breath sounds distinct. Expiration slightly prolonged over upper right. Many sonorous and sibilant rales over the whole right chest. Most plainly heard below the angle of the right scapula, where there is the suggestion of a friction sound. Few softer bronchial rales heard in the left axilla and the left upper chest posteriorly. Respirations wheezy and asthmatic."

These findings were confirmed by Dr. E. Quin Thornton, who gave the following opinion.

"There is evidently an inflammation of the bronchial system of the right side, with slight involvement of the left side."

This opinion was confirmed absolutely at bronchoscopy.



FIG. 3.—Bone that caused marked and typical asthmatic wheeze while lodged in right bronchus of a man, aged thirty-nine years. Removed bloodlessly through the mouth by bronchoscopy under local anesthesia. Though rales were still loud and numerous on ordinary auscultation after removal of the foreign body, the asthmatic wheeze, which had been so plainly audible at the open mouth, had totally disappeared. (Case No. Fbdy. 623.)

Remarks. In view of the negative radiograph and traumatic laryngotracheitis the question arose as to whether or not bronchoscopy should be done. The decision to do it at once was based largely on the asthmatic wheeze, which was so marked that it could be heard anywhere in the room when the patient had his mouth open. The wheezing sound had not the character of rales, evidently being produced by the foreign body itself and not by the attendant secretions. The wheezing was greater after expectoration than before.

The bone was removed bronchoscopically under local anesthesia in fifty-eight seconds, exclusive of the time required for applying the cocaine. Report of Dr. Spencer after removal of the foreign body:

"Wheezing respiration and the bronchial rales have disappeared. Respiratory sounds over the lower and middle right lobes somewhat

harsher, with respiration more prolonged than on the left side. Patient has no dyspnea and is very comfortable."

The patient was discharged the next day and made a complete and uneventful recovery.

Remarks. This may be regarded the next day and, as the leading case, though not chronologically first, in the establishment of the asthmatoïd wheeze, as an important diagnostic sign of foreign body in the bronchi. The radiograph was negative; the asthmatoïd wheeze was very loud; it was louder after effective expectoration;

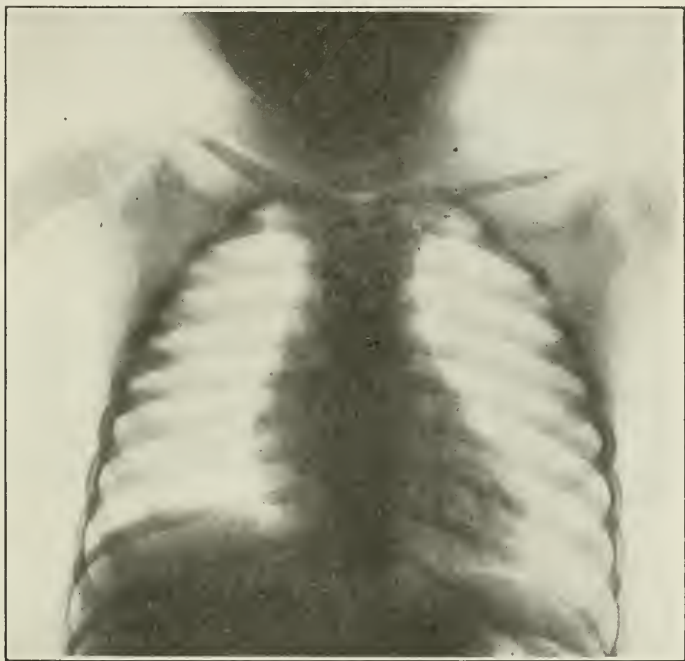


FIG. 4.—Radiograph showing eye of "teddy bear" in bronchus of a child, aged two years. Asthmatoïd wheeze was distinct and characteristic. (Radiographic plates made by Drs. Johnston and Grier. Case No. Fbdy. 583.)

bronchoscopy was done chiefly because of the asthmatoïd wheeze positive; the wheeze disappeared totally immediately after bronchoscopic removal of the foreign body. The irregular shape of the foreign body (Fig. 3) permitted air to pass through irregular spaces; its rough surface probably modified the sound.

CASE No. Fbdy. 583.—*Glass eye of "teddy bear" removed from the right stem bronchus by oral bronchoscopy; asthmatoïd wheeze present.* A girl, aged two years, aspirated half of the glass eye from a "teddy bear." The immediate symptoms were dyspnea and choking; later symptoms were coughing and wheezing. Physical examination

of the chest by Dr. Elterich showed a very much diminished amount of air was entering the right lower and middle lobes. On placing my ear to the open mouth of the patient the asthmatoïd wheeze was very plainly perceptible on expiration. A radiograph had been taken, but it failed to show the foreign body. The patient was then bronchoscoped, revealing the presence of the foreign body in the right bronchus, which, however, the operator was unable to remove. He referred the case to Dr. J. W. Cheney, of Wichita, Kansas, who referred the case to the author. A radiograph by Drs. Johnston and Grier showed not only the glass eye, but in addition the pupil of the eye was differentiated from the iris clearly in the radiograph (Fig. 4).



FIG. 5



FIG. 6

FIG. 5.—Glass eye of “teddy bear” that, when lodged in right bronchus (Fig. 3), caused a typical asthmatoïd wheeze. The angular cross-section permitted air to pass. The foreign body was removed bloodlessly through the mouth by bronchoscopy without anesthesia, resulting in the immediate disappearance of the asthmatoïd wheeze. (Case No. Fbdy. 583.)

FIG. 6.—Grain of maize that, in the bronchus of a child, aged five years, produced a typical asthmatoïd wheeze. The grain of corn was removed bloodlessly through the mouth by bronchoscopy without anesthesia, resulting in immediate disappearance of the asthmatoïd wheeze. (Case No. Fbdy. 579.)

Bronchoscopy, without anesthesia, general or local, promptly revealed the presence of the foreign body presenting in conoidal form. It required some manipulation properly to seize the foreign body for removal, the whole procedure from the time of the introduction of the bronchoscope requiring five minutes fifteen seconds. The wheeze disappeared totally after bronchoscopic removal of the foreign body (Fig. 5).

The child left for her home the next day and the recovery was complete and uneventful.

Remarks. It is not always easy to get a child of two years to coöperate in eliciting the asthmatoïd wheeze, but patience accomplished it in this case. It was plainly noticeable also when the child slept. The foreign body was of irregular shape, but its surface was smooth except for two sharp edges.

CASE No. Fbdy. 579.—*Grain of corn removed from the right bronchus by bronchoscopy; asthmatoïd wheeze present.* A girl, aged five years, was referred to me by Dr. J. W. Mayhew, of Lincoln, Nebraska, for the removal of a grain of corn aspirated while playing.

The immediate symptoms were violent coughing and dyspnea for about fifteen minutes. Later symptoms were occasional dyspnea and occasional coughing. Physical examination by Dr. F. T. Billings showed very much diminished expansion of the right lung during inspiration, with dulness on percussion all over the right chest. On placing my ear to the child's open mouth the asthmatoïd wheeze was plainly heard. It was much clearer after expectoration than before. Roentgen-ray examination was negative.

On passing the bronchoscope, without anesthesia, general or local, the grain of corn was seen impacted in the right bronchus, from which it was readily removed. Time required for the introduction of the bronchoscope and removal of the foreign body, two minutes fifty-four seconds. After bronchoscopy the asthmatoïd wheeze had altogether disappeared and all the abnormal physical signs were absent except some moist rales. The child left for home the next day and made a prompt and uneventful recovery (Fig. 6).

Remarks. In cases such as these the asthmatoïd wheeze is of very great importance because of the negative result of the radiograph. However, Dr. Mayhew had found the physical signs so strongly indicative of foreign body that he had advised the child coming over one thousand miles for the removal. It is not every diagnostician who feels so positive as to his diagnosis of foreign body in the lung.

CASE No. Fbdy. 560.—*Wooden whistle removed from left bronchus by oral bronchoscopy; asthmatoïd wheeze present.* A boy, aged eight years, was referred by Dr. Rush, of Portage, Pa., with a history of having aspirated part of a wooden whistle. A radiograph was entirely negative. Dr. H. T. Price found rales in the left chest, with very harsh breath sounds. His opinion was that there was a foreign body obstructing partially the entrance of air in the left lung. On placing my ear to the patient's open mouth a very distinct asthmatoïd wheeze was plainly heard on expiration. It was very much increased at the end of expiration when the patient forcibly expelled all that was possible of the residual air.

On passing the bronchoscope I found the wooden whistle (Fig. 7) tightly impacted in the left bronchus. I could see plainly into the tubular end, though momentarily obstructed by a small fragment of rubber still adhering to the whistle. An expanding forceps was inserted into the lumen of the whistle, which was then readily withdrawn. The child was discharged the next day and recovery was prompt and uneventful.

Remarks. The asthmatoïd wheeze in this case was not produced by any mechanism similar to that of a whistle. The foreign body consisted simply of a piece of wood, 3 cm. long by 8 mm. in greatest diameter, with a hole throughout the long axis. As a toy the sound is produced by the vibration of a rubber accessory. The asthmatoïd wheeze had a very slight cooing sound, possibly due to the smooth

round hole through which the air was passing. The asthmatoïd wheeze in this case was characteristic only at the end of prolonged and forced expiration.

CASE No. Fbdy. 386.—*Fish-bone removed from left inferior lobe bronchus by oral bronchoscopy. Asthmatoïd wheeze present.* A young woman, aged twenty-five years, was admitted to the Montefiore Hospital in Pittsburgh, with a wheezing respiration but no cyanosis. She stated that she had choked on a piece of fish-bone, the accident being followed by a severe attack of coughing. There were no other symptoms until about two weeks later, when she began to expectorate pus and the temperature began to go up a



FIG. 7



FIG. 8

FIG. 7.—Wooden cylinder (from toy whistle) that produced an asthmatoïd wheeze when lodged in the bronchus of a child, aged eight years. Removed bloodlessly through the mouth by bronchoscopy without anesthesia, resulting in immediate disappearance of the asthmatoïd wheeze. (Case No. Fbdy. 560.)

FIG. 8.—Fragments of fish-bone that produced a typical asthmatoïd wheeze when lodged in the left inferior lobe bronchus of a woman, aged twenty-five years. Removal by peroral bronchoscopy under local anesthesia resulted in immediate disappearance of the asthmatoïd wheeze previously heard on oral auscultation, notwithstanding rales were still audible on thoracic auscultation. (Case No. Fbdy. 386.)

little every day, the maximum being about 99.4° . Physical examination by Dr. Milton I. Goldsmith revealed decreased breath sounds over the left lung, with rales on both sides. Dr. Goldsmith's opinion was that there was a foreign body present. Dr. M. F. Goldsmith made excellent roentgen-ray plates which showed a slight shadow on the left side, though it could not be stated with certainty that the shadow was produced by a foreign body. When I was talking to the patient she seemed so markedly hysterical that I felt disinclined to believe there was any foreign body present. When, however, I examined her with the mirror very decided wheezing was noticeable, especially on expiration, slightly at times on inspiration also. The expiratory wheeze was much more marked after expectoration. Bronchoscopy was decided upon because of

the positive asthmatoïd wheeze. The bronchoscope was passed under local anesthesia and three pieces of fish-bone (Fig. 8) were removed from the left inferior lobe bronchus. Time of operation, three minutes thirty seconds, exclusive of time consumed in applying the cocain.

Remarks. The asthmatoïd wheeze was specially noticeable with mirror laryngoscopy. This is a very good way to elicit it in adults. The rales heard on both sides of the chest in this case, by Dr. Goldsmith, are quite common in foreign bodies lodged on one side. It seems that secretions produced by the presence of a foreign body in the bronchus of one side are aspirated into the bronchi of the other side. For this reason rales are very often not to be taken as indicative of the presence of foreign body on the side on which they are heard. Diminished air in one lung as compared to the other is, however, a localizing sign of great value.

CONCLUSIONS. 1. The asthmatoïd wheeze is a sound heard by placing the ear in front of the patient's mouth during expiration. It resembles the wheezing of the asthmatic patient, but is drier. It is caused by the vibration of the air passing the foreign body in the bronchus.

2. The asthmatoïd wheeze is elicited by oral auscultation, the ear of the examiner being placed close to the open mouth of the patient. In many cases it comes out clearly during mirror laryngoscopy in older children and adults.

3. The wheeze is most markedly elicited during forced and prolonged expiration. The best conception of the manner of elicitation will arise in an effort to expel the *residual* air from the lung. This is similar to the condition arising from a bechic series without any interval for an inspiration to renew the pulmonary air supply between coughs.

4. The sign is of less value if negative than if positive.

5. Being heard at the open mouth it is of no localizing value as to which lung is invaded, though there is hope that further study may develop perceptible differences between tracheally and bronchially lodged foreign bodies.

6. It is often more marked *after* coughing out of all the secretion of which the patient can rid himself, though this is not always the case, doubtless being influenced by the size and shape of the foreign body.

7. It is of more value directly as to the recent occurrence of the case. In cases of long-standing bronchitis, tuberculosis and other pulmonary lesions associated with abundant secretions there may be a wheezing audible on auscultation at the open mouth that may simulate the true asthmatoïd wheeze diagnostic of a foreign body in a recent case of foreign-body lodgment in a previously normal patient.

8. The asthmatoïd wheeze was not present in any case in which a smooth rounded body was so tightly wedged in a bronchus that no

air could pass it. Smoothness or roughness of surface seem important chiefly as they influence tightness of inspiration.

9. It is particularly desirable that this new physical sign of foreign body in the trachea and bronchi be tested for in every case and recorded present or absent in order statistically to determine its exact value.

10. In the author's opinion the asthmatoïd wheeze and oral auscultation are very promising additions to our diagnostic means in cases of foreign body in the trachea or bronchi.

A CONSIDERATION OF THE METHODS FOR DEMONSTRATING TUBERCLE BACILLI IN THE URINE.

BY ERNEST M. WATSON, A.M., M.D.,

BUFFALO, NEW YORK.

KLENCKE,¹ in 1843, was the first to successfully transmit tuberculosis into animals. His work, while taking priority, was by no means as extensive or painstaking as that of Villemin,² who some years later, in 1865, published a series of well-recorded and conclusive experiments of animal inoculations, with various materials of a tubercular nature. In 1867 Marcet³ was able to produce generalized tuberculosis in animals by inoculating urine from individuals suffering from renal-vesical tuberculosis. Peters,⁴ in 1872, successfully removed a kidney for tuberculosis, though the operation of nephrectomy had been accomplished some years previously by Simon,⁵ of Heidelberg, in 1869.

With the publication of the isolation and cultivation of the tubercle bacillus by Robert Koch,⁶ in 1882, the entire field of laboratory and clinical tuberculosis took upon itself an added impetus of study and accomplishment. Baumgarten⁷ had unquestionably seen the tubercle bacillus previously in tissues, but it remained for Koch to establish the epoch-making beginnings of the bacteriology of tuberculosis. Damsch,⁸ in the same year, 1882, began using the inoculation of guinea-pigs, with the urine of sus-

¹ Ueber die Contagiosität der Eingewurdewürmer nach Versuchen, und über das physiologische und pathologische Leben der mikroskopischen Zellen, nach empirischen Thatsachen, Zwei medizinische-physiologische Abhandlungen, iv, 420, 1, 1, Jena, 1884.

² Gaz. hebdom., 1865.

³ Tr. Med. Clin., 1867, p. 437.

⁴ Quoted by Walker, 1872: Johns Hopkins Hosp. Reports, 1904, vol. xii.

⁵ Quoted by Pilcher, 1869: Ann. of Surg., 1900, vol. xxxi.

⁶ Die Aetiologie der Tuberculose, Berl. klin. Wehnschr., 1882, xix, 221; Mitt. a. d. kais. Gesundheitsamr, 1884, ii, 1.

⁷ Virchows Arch., vol. lxxxii.

⁸ Die Impfbarkeit der Tuberculose als diagnostisches Hilfsmittel bei Urogenitaler Krankheiten, Deutsch. Arch. klin. Med., 1882, xxxi, 75.

pected individuals, to establish a diagnosis of renal tuberculosis. Babes,⁹ in 1883, was the first to find and demonstrate tubercle bacilli in the urine of patients suffering from genito-urinary tuberculosis. A few months later this work was confirmed by Rosenstein¹⁰ (1883).

The means used for the demonstrating of tubercle bacilli in the urine have been until comparatively recent years the simple settling of the sediment by natural gravitation over a period of hours or by centrifugalization of the same. From this sediment a few loopfuls of material were smeared on a glass slide, fixed in the flame and stained in the earlier days by the anilin-water-gentian-violet method of Ehrlich,¹¹ but more recently by the carbol-fuchsin solution of Ziehl.¹² The simple gravity method is still the one most generally used, and as an example of the same may be mentioned the technic of Walker, who, in an exhaustive study of renal tuberculosis, was able to demonstrate the tubercle bacilli in each of the 50 cases studied by him.

1. WALKER'S METHOD:¹³

(a) The specimen of urine is allowed to settle in a conical urine glass for twelve hours.

(b) Six slides are then prepared, free from fat, as follows: boil for thirty minutes in a strong solution of caustic soda, which is then washed off with running water for another thirty minutes. The slides are then wiped dry with a clean linen cloth.

(c) The sediment from the conical glass is then taken up by means of a pipette and two drops placed on each slide.

(d) The slides are then put on a frame, about ten inches above a Bunsen flame, which is turned sufficiently low to prevent too rapid heating. They are allowed to remain until all of the fluid has evaporated and they have become perfectly dry.

(e) The slides are then passed through the flame in the ordinary manner, so as to fix the specimens thoroughly.

(f) They are then placed in 5 per cent. acid (HCl) alcohol and allowed to remain for five minutes. This procedure dissolves the urinary salts.

(g) The slides are next washed very carefully in running water, to remove all traces of acid and alcohol.

(h) The smears are now stained for ten minutes in carbol-fuchsin and decolorized with Gabbet's blue.

⁹ Nachweis des Tuberkelbacillus im Urin bei Tuberculose des Uro-genital Apparatus (trans. from Orbosi Netil, 1883, No. 7, extr.), Pest. med. Chir., xix, 219, Presse, Budapest, 1883.

¹⁰ Vorkommen des Tuberkelbacillen im Harn. Centralbl. f. d. med. Wissensch., Berlin, 1883.

¹¹ Ueber provocirte Fluorescenz erscheinungen am Auge, Deutsch. med. Wehnschr., 1882, viii, 21, 35, 54.

¹² Ueber die Farbung des Tuberkelbacillus, Deutsch. med. Wehnschr., 1883, ix, 247.

¹³ Renal Tuberculosis, Johns Hopkins Hosp. Reports, 1904, vol. xii.

(i) The whole field is then carefully gone over.

The next definite advance in the procedure of demonstrating tubercle bacilli in the urine was made by Uhlenhuth, who, in 1908, employed antiformin (equal parts of liquor chlorinatæ and sodium hydroxide, 15 per cent.) to dissolve and destroy the excess of pus and mucus and epithelial cells in the urine.

2. UHLENHUTH'S METHOD:¹⁴

(a) The specimen of urine is centrifuged in the ordinary manner for thirty minutes.

(b) The supernatant fluid is then poured off and the remaining sediment treated with antiformin in the proportion of 1 to 4 or 1 to 2 and the mixture stirred until an absolutely homogeneous mass is obtained.

(c) The specimen is then again centrifuged for ten minutes.

(d) The supernatant fluid is then poured off and the sediment washed two or three times with physiological salt solution, each time followed by centrifugalization and decanting.

(e) Smears are then made on glass slides from the remaining sediment and allowed to dry in the air.

(f) These are then fixed by passing through the Bunsen flame in the usual manner.

(g) The fixed smears are next stained with carbol-fuchsin by heating over a flame for ten minutes decolorized with acid and then alcohol (2 per cent. HCl) until all traces of the fuchsin are removed. They are then counterstained with Loeffler's methylene blue.

(h) The entire field of each slide is then carefully examined.

In the same year another method was devised by Ellerman and Erlandsen, having for its main object the destruction of the extraneous organic matter in the specimen, such as pus, mucus, etc. In this respect this method was similar to that of Uhlenhuth's, except that this action was brought about by incubation and digestion rather than by strong alkaline destruction.

3. ELLERMAN AND ERLANDSEN'S METHOD:¹⁵

(a) The urine is drawn by a catheter and allowed to settle for several hours.

(b) The supernatant fluid is then decanted and 10 to 15 c.c. of the sediment is centrifugalized and the supernatant fluid decanted. (In case of unusual proportions of urates they are removed by heat before centrifugalizing.)

(c) The sediment is then mixed with four times its bulk of a 0.25 per cent. solution of sodium carbonate and 0.25 to 0.50 gm. of pan-

¹⁴ Intiformin. ein bakterien auf losendes Desinfektionemittel, Berl. klin. Wehnschr., 1908, xlv, 1346.

¹⁵ Nachweis von Tuberkelbazillen in sputum. Studien über die physikalischen Verhältnisse bei verschiedenen Homogenisierungs und Sedimentierungsmethod-neue methoder, Ztschr. f. Hygiene u. Infectiouskrankh., 1903, Band lxi, 219. Om en rationel Fremgangs maade til Pa avising of Tuberkelbacillen i urinem, Hospitalstidende, 1908, No. 30, p. 873.

creatin and allowed to incubate for twenty-four hours at 37°. If the reaction is still acid it may be necessary to add more sodium carbonate and allow the digestion to continue somewhat longer.

(d) The upper layer of the supernatant fluid is then decanted and the rest again centrifugalized.

(e) To the remaining sediment, after again decanting, is added four times its volume of a 0.25 per cent. solution of sodium hydroxide and stirred with a glass rod until dissolved.

(f) The whole is then heated to boiling over a water-bath for several minutes. On cooling it is once more vigorously centrifugalized and the sediment obtained is used for microscopic study.

(g) From the last-obtained sediment smears are made on glass slides and stained with carbol-fuchsin, decolorized in acid alcohol and counterstained in Loeffler's methylene blue, as in the method of Uhlenhuth.

Some time later, in 1909, Lange and Nitsche advocated a little different procedure in which they employed ligroine¹⁶ added to the specimen. Their experiments showed that the acid-fast bacilli adhered more closely to ligroine than did the non-acid-fast organisms, and so with this hydrocarbon added the tubercle bacilli could be found adherent to the surface of the above medium. Their method was as follows:

4. LANGE AND NITSCHÉ'S METHOD:¹⁷

(a) The urine is allowed to sediment by gravity for several hours or an amount is centrifuged until a reasonable sediment is obtained and the supernatant fluid decanted.

(b) The sediment is then mixed with a solution of caustic soda in proportion of 1 to 4 and allowed to incubate at 37° until the mixture is perfectly homogeneous.

(c) The specimen is then diluted with an equal amount of sterile water and stirred vigorously, after which 2 c.c. of ligroine is added to the mixture.

(d) The specimen is stirred vigorously again and heated over a water-bath to 65° C. until it separates into two layers: (1) the upper layer of ligroine, and (2) the lower of urine, caustic soda and water.

(e) The tubercle bacilli are found in the ligroine solution and a few drops of this upper layer are placed on several slides, which are allowed to dry in the air.

(f) The specimens are then fixed in the Bunsen flame and stained with carbol-fuchsin, decolorized with acid alcohol and counterstained with Loeffler's methylene blue in the usual manner.

Taking advantage of the layer method above described, Kozlow,

¹⁶ Ligroine is a hydrocarbon of the homologues of methane obtained by collecting the portion of petroleum that boils between 80 and 120°. It is somewhat similar to naphtha, gasolin and benzin.

¹⁷ Eine neue Methode des Tuberkelbazillen nachweises, Deutsch. med. Wehnschr., 1909, xxxv, 435.

in 1910, practised a little different procedure, which has since met with considerable success. His method combined both the advantages of antiformin as a solvent for the organic matter and the layering of different fluids to obtain the acid-fast organisms at a given level.

5. KOZLOW'S METHOD:¹⁸

(a) 20 to 30 c.c. of urine are taken to which is added 1 c.c. of antiformin for every 5 c.c. of urine.

(b) This is shaken for thirty minutes, to render the mixture homogeneous.

(c) To the specimen is then added twice its volume of sterile water and twice its volume each of ether and acetone.

(d) The mixture thus obtained is then shaken for five seconds and allowed to stand for one minute.

(e) On standing the specimen is composed of three layers: (1) the upper portion of ether; (2) the middle of bacteria; (3) the lower of water, antiformin and acetone.

(f) A few drops from the middle layer are then placed on glass slides and allowed to evaporate in the air.

(g) The slides are then fixed in the Bunsen flame, stained with carbol-fuchsin, decolorized with acid alcohol and counterstained with Loeffler's methylene blue.

A somewhat more simple procedure, advocated by Brown, in 1915, and in use at the Saranac laboratories, is the method of Petroff. This depends in its efficacy on the precipitation of the urine, which precipitate carries down with it the organisms and so makes them easier to find.

6. PETROFF'S METHOD:¹⁹

(a) The urine specimen for examination is first acidified with 30 per cent. acetic acid.

(b) To the acidified urine is then added 2 per cent. of its volume of a 5 per cent. solution of tannic acid.

(c) The urine is then placed in an ice-chest for twenty-four hours and the precipitate allowed to settle.

(d) The supernatant fluid is then decanted and the precipitate is centrifugalized.

(e) The centrifugalized sediment and precipitate is then used to prepare several slides.

(f) These are dried in the air and stained in the usual manner with carbol-fuchsin, decolorized with acid alcohol and counterstained with Loeffler's methylene blue.

A more recent procedure, advocated by Crabtree and depending

¹⁸ Antiformin and its Preparation: The Ether-acetone Combination of the Antiformin Method. On the Value of Demonstrating Tubercle Bacilli in the Blood, *Kazan. Med. Jour.*, 1910, No. 10, p. 95. Aether-acetonische Kombination der Antiformin methode, *Berl. klin. Wehnschr.*, 1910, xlvii, 1181. Roussky Vratsh, 1910, No. 22.

¹⁹ The Significance of Tubercle Bacilli in the Urine, *Jour. Am. Med. Assn.*, March 13, 1915, lxiv, 886.

in its efficacy on the different specific gravity of the acid-fast organisms compared with the ordinary bacteria and the organic matter usually present, *i. e.*, pus, epithelial cells, mucus, etc., is one that may be termed fractional centrifugalization.

7. CRABTREE'S METHOD:²⁰

(a) The specimen for examination is placed in the centrifuge and allowed to spin for one or two minutes at low speed.

(b) The supernatant urine is then decanted into a clean test-tube and the sediment discarded (this contains pus, mucus, epithelial cells and the ordinary bacteria if present).

(c) The urine specimen is then centrifuged for fifteen to thirty minutes or until clear.

(d) The supernatant fluid is then decanted and discarded and the tube refilled again and centrifuged. This procedure is repeated two or three times.

(e) After the final centrifugalization the supernatant urine is poured off and the tube containing the sediment inverted.

(f) After draining the remaining sediment is used to make smears in the ordinary manner, which are allowed to dry in the air.

(g) These are then fixed in the Bunsen flame and stained with carbol-fuchsin, decolorized with acid alcohol and counterstained with Loeffler's methylene blue.

After a thorough and painstaking study of the various methods of demonstrating tubercle bacilli in the urine which were available at that time, Seminov,²¹ in 1911, came to the conclusion that the method of Kozlow was uniformly the most reliable for the simple demonstration of organisms. For enrichment tests and the finding of organisms in larger numbers, however, he concluded that the method of Ellerman and Erlandsen yielded perhaps the best results.

In the examination of urine for tubercle bacilli the method which requires the fewer laboratory reagents consumes less time and gives a higher percentage of positive results is the one which will be used eventually. In studying numerous specimens for the presence of acid-fast organisms in various conditions of urogenital tuberculosis the writer has found that one important factor not previously given much attention is to use large amounts of urine, also to keep the specimen in the original container until the final sediment is obtained and to centrifugalize thoroughly. The following procedure has been found to give excellent results.

8. METHOD:

(a) Irrigate the glans penis and urethra with sterile water (this eliminates the smegma bacillus and other extraneous organisms).²²

²⁰ A Method of Demonstrating Bacteria in the Urine by Means of the Centrifuge, *Surg., Gynec. and Obst.*, February, 1916, xxii, 221.

²¹ Valeur comparative des procedes pour deceler et color les bacilles tuberculeux dans l'urine, *Presse Médicale*, October 14, 1911, No. 82, p. 820.

²² The Possibility of Avoiding Confusion by the Smegma Bacillus in the Diagnosis of Urinary and Genital Tuberculosis, *Am. Jour. Med. Sc.*, July, 1905, cxxx, 52.

(b) The patient then voids in three glasses. The last is a conical-shaped sedimenting glass of 250 c.c. capacity and fits in an ordinary high-powered electric laboratory centrifuge. If the patient is unable to void the required amount the specimen is set aside under sterile conditions and the process of urinating in three glasses is repeated until the required amount, *i. e.*, 200 c.c., is obtained. (If desired the patient may be catheterized and the entire specimen used for study; this is particularly desirable in the female.)

(c) The specimen (about 200 c.c.) is then placed in the electric centrifuge and revolved for five minutes at moderate speed. If there is much sediment, 5 c.c. of antiformin is added and the specimen is thoroughly stirred for several minutes, with a sterile glass rod, until a perfectly homogeneous mixture is obtained. (If there is very little sediment it is not advisable to use antiformin. Some definite macroscopic sediment is highly desirable, for it acts as a fixative and facilitates focusing in searching for organisms.)

(d) The entire specimen is then subjected to a second centrifugalization at high speed for thirty to forty-five minutes.

(e) The supernatant urine is then decanted and the sediment at the bottom or apex of the cone is used for preparing three glass slides.

(f) The slides are allowed to dry in the air and fixed in the Bunsen flame.

(g) If the smears appear thick to the eye they are placed in 5 per cent. acid (HCl) alcohol for two minutes. This procedure dissolves the urinary salts, which, if stained by the fuchsin, are often confusing, after which they are again fixed in the Bunsen flame.

(h) The slides are then stained in carbol-fuchsin for ten minutes. The entire slide is submerged in the stain and heat is applied until the solution steams. The slides are then washed in running water and placed in 2 per cent. acid (HCl) alcohol until completely decolorized. They are then counterstained in Loeffler's methylene blue.

An important point mentioned by Churchman²³ is that if negative results are obtained in a specimen from a suspected case of vesical tuberculosis a thorough irrigation of the bladder, with moderate distention and careful examination of the bladder washings, should be carried out. An ulcer in the vertex or high on the anterior bladder wall may thus shed organisms into the irrigating fluid when the urine is negative.

If the attempts to demonstrate the offending organisms in cases of suspected urogenital tuberculosis have yielded no results, resort may be had to animal inoculation. This method was first used by Damsch in 1882 and has in recent years come into quite general use. In the earlier days the six weeks essential for the disease to become generalized in guinea-pigs was definitely a drawback to its

²³ Notes on the Examination of Urine for Tubercle Bacilli, *AM. JOUR. MED. SC.*, November, 1914, No. 5, cxlviii, 722.

extensive employment. Bloch,²⁴ in 1907, was able to shorten this period considerably by mechanically injuring the inguinal lymph glands in guinea-pigs previous to inoculation and then injecting 1 c.c. of urine subcutaneously in the inguinal region. By this method he was able to demonstrate tuberculous inguinal lymph nodes in from nine to eleven days after inoculation in positive cases.

Following along the work of Heineke²⁵ and of Murphy and Ellis,²⁶ who showed the susceptibility of lymphoid tissue to infection after exposure to the roentgen-rays, Morton,²⁷ in 1916, advocated the routine inoculation of the roentgen-rayed guinea-pig as a laboratory test for urogenital tuberculosis. Morton demonstrated that in from eight to ten days in such animals, pathological studies showed tubercular lesions.

By making use of all the laboratory methods at our disposal, however, we are not always able to demonstrate the presence of tubercle bacilli in all cases. The guinea-pig test is not infallible, as shown by the reports of Terry²⁸ and of Barney and Young,²⁹ and occasionally the organisms may be demonstrated by centrifugalization and staining when the guinea-pig test is negative.

BLOOD-PRESSURE AND KIDNEY FUNCTION FINDINGS IN ORTHOSTATIC ALBUMINURIA.¹

BY E. H. MASON, M.D.,

AND

R. J. ERICKSON, M.D.,

MONTREAL, CANADA.

(From the Medical Clinic of the Royal Victoria Hospital, Montreal.)

WITHIN recent years considerable interest has been shown in the peculiar condition for which Tessier,² in 1899, proposed the name of "orthostatic albuminuria." This condition has also several other names, such as cyclic, postural, intermittent and physiological albuminuria, but none of these convey such an exact meaning of the

²⁴ Nachweis des Tub.-bac. durch den Tierversuch, Berl. klin. Wchnschr., 1907, No. 17, xlv, 509.

²⁵ Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen auf innere Organe, Mitt. a. d. Grenzgeb. d. Med. u. Chir., Jena, 1904-1905, xiv, 21.

²⁶ Experiments on the Role of Lymphoid Tissue in the Resistance to Experimental Tuberculosis in Mice, Jour. Exper. Med., 1914, xx, 397.

²⁷ A Rapid Method for the Diagnosis of Renal Tuberculosis by the Use of the Roentgen-rayed Guinea-pig, Jour. Exper. Med., 1916, xxiv, 419.

²⁸ Specimens of Tuberculosis of the Kidney in which the Guinea-pig Test was Negative, Boston Med. and Surg. Jour., February 16, 1917.

²⁹ The Value of the Guinea-pig Test in Genito-urinary Tuberculosis, Boston Med. and Surg. Jour., January, 1911, clxiv, 917.

¹ We wish to acknowledge our appreciation of a grant from the James Cooper Fund of McGill University, which has made this work possible.

² Semaine Méd., 1899, xix, 425.

true disturbance as orthostatic albuminuria. In brief, such cases are those that show the presence of serum albumin in the urine when in the erect position, which albumin completely disappears upon assuming the recumbent position.

Orthostatic albuminuria has been recognized for many years, but of the exact nature of the disturbance we still remain in ignorance. It is equally common among young people of both sexes, most of the cases falling between the sixteenth and twenty-second years. Previously males were thought to be more susceptible to the condition than females, but now we know that to be untrue. Lommel states that the condition is present in varying degrees in about 19 per cent. of adolescents between fifteen and twenty-one years of age. The condition, as a rule, occurs in poorly nourished anemic individuals, they being usually rather lean in appearance and showing certain manifestations of vasomotor instability. It is often possible to trace its presence through several generations, and Lacour reports its occurrence in three children in the same family.

The amount of serum albumin that appears in the urine when in the upright position varies greatly, by far the largest number showing only a trace with heat and acetic acid while a few show as much as 5, 6 and even to 10 grams per liter. As a rule, serum globulin is not present. The albumin may or may not be accompanied by casts or cylindroids. Usually they are not present, but cylindroids are of slightly greater frequency than casts. Jehle³ reported 1 case in which casts and red blood cells were present with the albumin. The albuminuria usually reaches its maximum in the forenoon, decreasing during the afternoon hours. The amount present has little relation to exercise except that there seems to be a tendency for traces to disappear in mild cases which can be accounted for by the associated increased pulse-pressure. Exercise while in the recumbent position never produces an albuminuria.

Quantitative examinations of the urine excreted fail to show any abnormality (Archard,⁴ Merklen and Claude⁵). This is confirmed by the following nitrogen partition in one of our cases:

Serial No. 1; Medical No. 24505. Date: November 1, 1916.
Twenty-four-hour urine: 700 c.c.

	Per cent.	Gm. per 24 hours.	Percentage of total nitrogen.
Total N.	0.901	6.307	
Urea N.	0.724	5.068	80.4
Ammonia N.	0.046	0.322	5.1
Creatinine N.	0.273	4.3
Uric acid N.	0.163	2.6
Rest N.	0.481	7.6
Urea	1.551	10.857	
Ammonia	0.056	0.392	
Creatinine	0.105	0.735	
Creatin	0	0	
Uric acid	0.070	0.490	

³ *Ergebn. d. inn. Med. u. Kinderheilk.*, 1913, xii, 808.

⁴ *Compt. rend. Soc. méd. d. hôp.*, June 22, 1900.

⁵ *Ibid.*, July 27, 1900.

The three theories of the cause of orthostatic albuminuria which have received the greatest consideration are:

1. A developmental defect of glomeruli resulting in their increased permeability (Tessier).⁶

2. Vasomotor instability, the albuminuria being due to a diminished pulse-pressure (Erlanger and Hooker).⁷

3. A mechanical interference with the renal circulation, due to increased lordosis (Jehle).⁸

THE THEORY OF TESSIER. The argument of Tessier was advanced in 1905 but has never met with much approval, as it is based upon no demonstrable facts. It is true that these people are often poorly developed, especially their arterial systems, and many of them have a small heart and a subnormal body weight. In this connection Leube calls it the albuminuria of adolescence, explaining it as being due to a slight inability on the part of the kidney to keep pace with the rest of the growing organism. As the patients become older a readjustment takes place or the temporary insufficiency is improved, as shown by the disappearance of the albuminuria, with mature years. Other evidences of faulty development are also commonly found, such as varying degrees of general visceroptosis, shown by the roentgen rays, and easily palpable kidneys. Bass and Wessler⁹ found that 30 per cent. in a series of thirty-six children with orthostatic albuminuria showed hearts of the "drop type," and many of them showed other signs of maldevelopment.

THE THEORY OF ERLANGER AND HOOKER. The work of Erlanger and Hooker in 1904 resulted in the presentation of the vasomotor instability theory, the cause of the albuminuria being due to the low pulse-pressure present when they assume the upright position. We know that when a normal person assumes the upright position the pulse-pressure becomes smaller, but in cases of orthostatic albuminuria the decrease is much more marked. In normal persons the maximum and minimum pressures always tend to approach each other, but there may be either a raising or a dropping of the maximum pressure. In cases of orthostatic albuminuria the maximum pressure usually remains constant and the change takes place in the minimum pressure. This is well shown in the reported cases. Edel¹⁰ has presented some evidence which shows there is a loss of control of the cardiovascular system on the part of the vasomotor system, resulting in the former's inability to respond to ordinary changes. His cases failed to show the usual rise in pulse-pressure after a warm bath and cold sponges. Exercise, such as climbing stairs, had much less influence upon pulse-pressure than in a normal

⁶ *Revue der méd.*, 1905, xxv, 233.

⁷ *Johns Hopkins Hosp. Repts.*, 1904, xii, 145.

⁸ *München. med. Wchnschr.*, 1908, lv, 12.

⁹ *Arch. Int. Med.*, 1913, xi, 403.

¹⁰ *Ibid.*, 1914, xiii, 39.

individual. As early as 1886 Craig¹¹ offered the suggestion that the albumin was present in the urine as the result of low arterial tension, and he claimed that he could cause the albuminuria to disappear by raising the blood-pressure. Bass and Wessler,¹² in their 36 children, came to the conclusion that the hearts of the children failed to become smaller after exercise which they believed to be due to a partial loss of the nervous control resulting in limited cardiac response.

Erlanger and Hooker¹³ in their studies on pulse-pressure, arrived at the following conclusions:

1. Amount of urine secreted varies directly with the magnitude of pulse-pressure.
2. In a case of orthostatic albuminuria the amount of albumin in the urine varies inversely as the magnitude of pulse-pressure.
3. Urea, chlorides and phosphates secreted in the urine vary directly with the magnitude of pulse-pressure.

Again, Gesell¹⁴ showed that with the same volume of flow through the kidney and a diminished pulse-pressure the nutrition of the kidney cells would be altered. The higher pulse-pressures give the kidney more massage, for we know that mechanical shock greatly influences the functions of protoplasm. This was well shown by Kahlenberg¹⁵ in dialyzing solutions through osmotic membranes. Only when stirring takes place (mechanical shock) can the maximum osmotic pressure be obtained. Again, a pulsating fluid is better able to penetrate into every part of an organ than one driven by a constant pressure. The diminished pulse-pressure also interferes with the gaseous exchange in the kidneys, as shown by Fleisheel v. Marxow.¹⁶ Accordingly the nutrition of the kidney cells is interfered with. These facts all point toward the lowered pulse-pressure as upsetting the normal metabolic processes of the renal cells as well as those of the glomeruli, which allows them to become permeable to serum albumin and at the same time alters their function.

THE THEORY OF JEHLÉ. In 1908 Jehlé¹⁷ advanced the mechanical theory, based upon the presence of an increased lordosis, which is often present. The lordosis is usually found at the level of the twelfth dorsal and first and second lumbar vertebræ, and interferes with the venous return of blood from the kidneys when exaggerated by the upright position. Experimentally, Jehlé was able to cause the albumin to disappear by correcting the lordosis while in the upright position, but coincident pulse-pressure observations are lacking. This could be done either by abdominal support or by raising one leg on a chair. Also, he was able to produce albuminuria

¹¹ British Med. Jour., 1886, i, 333.

¹³ Loc. cit.

¹⁵ Jour. Physiol. Chem., 1906. No. 3, x.

¹⁶ Beitrage zur Phys. zu Ludwig gewidmet, 1887, p. 29.

¹² Loc. cit.

¹⁴ Am. Jour. Physiol., 1913, xxxii, 70.

¹⁷ Loc. cit.

in normal individuals by artificially producing lordosis and by pressure upon the larger venous trunks through the abdominal wall. Notlmann confirmed Jehle's work as regards the production of albuminuria by artificially produced lordosis as well as to lower pulse-pressure by artificially produced lordosis while in the horizontal position. Muscular exercise, while in the horizontal position, fails to cause albumin to appear in the urine (Guilblain¹⁸).

It is well known how sensitive the renal cells are to slight changes in their nutrition. Jehle believes that the passive congestion from which the kidneys suffer when the lordosis is exaggerated interferes with their nutrition. This retarded circulation interferes with the cells food supply and with the removal of their waste products in a similar manner as when caused by a lowered pulse-pressure. It is known that the epithelium of the glomeruli is more sensitive to agents that increase its permeability than that of the convoluted tubules. This diminished blood flow through the kidney causes the excretion of a small amount of highly concentrated urine, which concentration is not in proportion to the oliguria.

During the last year we have had the opportunity to study 5 cases of orthostatic albuminuria, 4 of which are quite typical. Our observations that are of special interest have been made upon pulse-pressure and kidney function when in different positions. A brief synopsis of each case follows, after which the special findings are given in more detail.

Serial No. 1; Medical No. 24505. Male, aged eighteen years. Admitted to the Royal Victoria Hospital September 4, 1916, complaining of "discomfort in the pit of the stomach."

Present Illness. For many years has had headaches, with occasional spells of nausea and vomiting. Since March, 1916, has had a feeling of distress in his epigastrium, which comes on about one and a half hours after all meals. This distress continues until he eats his next meal, when it disappears for a short time. Chronically constipated for as long as he can remember and has lost twenty pounds in weight since March, 1916. No urinary symptoms.

Personal History. A weak child; no history of scarlet fever or of other kidney involvement.

Family History. Unimportant.

Present Condition. The young man is thin, lanky, poorly developed; weight, 92 pounds. Mucous membranes are pale.

Lymphatic System. Tonsils greatly enlarged, but there is no general glandular enlargement.

Respiratory System. Thorax is long, thin and flat, but symmetrical. Expansion is good.

Cardiocirculatory System. Pulse is of a low tension and vessel walls are not palpable. The heart is small and tends to be of the "drop type."

¹⁸ Arch. Int. Med., 1910, v, 491.

Digestive System. The abdomen is scaphoid. The liver is palpable one finger's breadth below the costal margin. The spleen is not palpable. The right kidney is easily palpable when in the upright position.

Genito-urinary System. Normal.

Locomotor and Integumentary Systems. The muscular development is poor and the muscles are of poor tone. There is marked mobility of the lower dorsal and lumbar spines; when standing the normal lordosis is considerably exaggerated.

Nervous System. Normal.

Blood. Red blood cells, 4,320,000; hemoglobin (Sahli), 72 per cent.; white blood cells, 8200.

Gastric Analysis. September 8, 1916. The preliminary lavage was clear. One hour after a test-meal 50 c.c. were removed. Reaction acid. The total acidity was 71, with a free HCl of 43. There were neither lactic acid nor blood present. Microscopically the findings were normal.

Urine. The urine failed to show casts or cylindroids at any time.

Radiological Report. Marked general visceroptosis. Heart narrow and long. Marked ptosis and atony of stomach. Extreme splenic and hepatic flexure acuity.

NOTE.—This case was treated by a spinal brace, with an abdominal support. On June 6, 1917, when wearing his brace, his urine contained no albumin when voided in the upright position. General condition had greatly improved.

Serial No. 2; Medical No. 24684. Male, aged forty-three years. Admitted to the Royal Victoria Hospital October 12, 1916, complaining of indefinite pains in the stomach, constipation and weakness.

Present Illness. Since March, 1916, he has felt tired, has had no appetite and has been very constipated. At times he has experienced a sensation of food sticking in the epigastrium after meals, which would be followed by some belching of gas. Has been very nervous and has lost 20 pounds in weight within the last six months.

Personal History. Unimportant.

Family History. There is an indefinite history of "kidney disease" in the father and in one sister.

Present Condition. He is a poorly developed, undernourished, hypersensitive Jew. Muscles are flabby and mucous membranes are pale. Weight 112 pounds.

Lymphatic System. Normal.

Respiratory System. Chest is long and flat. Expansion is poor and at both apices there are signs of an early tuberculous process.

Cardiocirculatory System. Heart rather small and pulled down by a sagging diaphragm.

Digestive System. No abdominal organs are palpable. Upon standing there is considerable bulging of the lower quadrants.

Genito-urinary System. Normal.

Locomotor and Integumentary Systems. When standing there is a slightly increased lordosis.

Nervous System. Reflexes increased.

Blood. Red blood cells, 4,040,000; hemoglobin (Sahli), 58 per cent.; white blood cells, 15,000. Blood-pressure (lying): systolic, 138; diastolic, 88.

Gastric Analysis. Normal.

Urine. Showed no casts at any time.

Radiological Report. Gastro-enteroptosis. Ileal and colonic stasis.

Serial No. 3; Medical No. 25406. Female, aged twelve years. Admitted to the Royal Victoria Hospital March 12, 1917, complaining of "epileptic fits," headaches and constipation.

Present Illness. Since nine years of age she has had "fits" once or twice a week. After each one she suffers from a headache. Has been constipated for five years. No urinary symptoms.

Personal History. When eleven months old had "spinal fever," after which she was paralyzed for several months.

Family History. Unimportant.

Present Condition. She is a moderately well-developed young girl; weight, 94 pounds. The physical examination is negative except for a slightly exaggerated lordosis and a palpable right kidney when standing. The *urine* at no time contained casts or cylindroids.

Serial No. 4; Medical No. 25678. Male, aged twenty years, admitted to the Royal Victoria Hospital April 28, 1917. There were no complaints as the condition was discovered during a life insurance examination.

Personal History. For several years his lower back has been rather easily tired after physical work. Occasionally has headaches and is constipated. There have been no urinary symptoms.

Family History. Unimportant.

Present Condition. He is a rather lanky young man of only fair muscular development. The lower dorsal and lumbar spines are very flexible, and when in the upright position the normal lordosis is considerably increased. The lower pole of the right kidney is palpable when standing, otherwise the physical examination is negative. Weight, 137 pounds.

The *urine* contained no casts or cylindroids.

Serial No. 5; Medical No. 25649. Female, aged twenty-one years, admitted to the Royal Victoria Hospital April 22, 1917, complaining of indefinite pains across the lower back, headaches and dizzy sensations.

Present Illness. Since August, 1916, has suffered from a dull, aching sensation over the lumbar region, especially in the right side, headaches and flushing of face. Infrequently has experienced dizziness on rising in the morning. There has been slight nycturia for the last five years but no polyuria or dysuria. Bowels are regular.

Personal History. Normal except for a right-sided pleurisy, with effusion one year ago, which was considered to be tubercular.

Family History. Unimportant.

Present Condition. She is a rather thin, flexible girl, with a fair muscular development. Spine is excessively mobile, and when in the upright position the normal degree of lordosis is considerably increased. Mucous membranes are pale. Weight, 116 pounds, otherwise physical examination is negative except for a palpable right kidney (lower pole) when standing.

Fluoroscopic Examination. Shows heart to be long and thin.

Urine. Cylindroids were found on one examination. Casts were not found.

Blood-pressure. Blood-pressure observations were made upon 4 of these 5 cases as well as upon 3 cases of acute nephritis, 1 case of chronic diffuse nephritis and upon several other ward cases whose troubles were not referable to their kidneys. All estimations were made with a Nicholson mercury instrument with a 11.5 cm. arm band. As the findings proved to be of such interest they are given in full:

Serial No. 1; Medical No. 24505. (Average of three estimations.)

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	94	55	39
II. Sitting: feet up	93	74	19
III. Sitting: feet down	94	74	20
IV. Standing	94	80	14
V. Standing: with brace	94	80	14

Serial No. 2; Medical No. 25406. (Average of two estimations.)

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	115	55	60
II. Lying with two pillows in small of back	112	80	32
III. Standing	112	80	32
IV. Standing up against wall	112	78	34
V. Standing with one leg raised at right angles to trunk	112	75	37

Serial No. 4; Medical No. 25678. (Average of two estimations.)

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	130	84	46
II. Lying with two pillows in small of back	130	84	46
III. Standing	130	90	40
IV. Standing up against wall	128	90	38
V. Standing with one leg raised at right angles to trunk	128	86	42

Serial No. 5; Medical No. 25649. (Average of two estimations.)

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	140	55	83
II. Lying with two pillows in small of back	140	80	60
III. Standing	140	85	55
IV. Standing up against wall	140	85	55
V. Standing with one leg raised at right angles to trunk	140	80	60

The following are the findings in the 3 cases of acute nephritis:
Medical No. 25374.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	124	60	64
II. Lying with two pillows in small of back	124	64	60
III. Standing	115	74	41
IV. Standing up against wall	117	70	47
V. Standing with one leg raised at right angles to trunk	120	73	47

Medical No. 24738.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	120	75	45
II. Lying with two pillows in small of back	115	85	30
III. Standing	115	95	20
IV. Standing up against wall	115	88	27
V. Standing with one leg raised at right angles to trunk	115	90	25

Medical No. 24890.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	115	62	53
II. Lying with two pillows in small of back	118	62	56
III. Standing	118	88	30
IV. Standing up against wall	115	78	37
V. Standing with one leg raised at right angles to trunk	120	75	45

The remaining cases follow with their diagnoses:
Medical No. 25604. Diagnosis: chronic diffuse nephritis.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	115	80	35
II. Lying with two pillows in small of back	112	80	32
III. Standing	116	84	32
IV. Standing with one leg raised at right angles to trunk	115	86	29

Medical No. 25705. Diagnosis: chlorosis.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	102	66	42
II. Lying with two pillows in small of back	99	60	39
III. Standing	94	56	38
IV. Standing with one leg raised at right angles to trunk	102	60	42

Medical No. 25702. Diagnosis: diabetes mellitus.

	Systolic.	Diastolic.	Pulse- pressure.
Position: I. Lying	139	78	61
II. Lying with two pillows in small of back	138	81	57
III. Standing	138	89	49
IV. Standing with one leg raised at right angles to trunk	138	78	60

Medical No. 25410. Diagnosis: diabetes mellitus.

	Systolic.	Diastolic.	Pulse-pressure.
Position: I. Lying	141	80	61
II. Lying with two pillows in small of back	135	85	50
III. Standing	138	85	53
IV. Standing with one leg raised at right angles to trunk	138	87	49

Medical No. 25738. Diagnosis: visceroptosis.

	Systolic.	Diastolic.	Pulse-pressure.
Position: I. Lying	128	80	48
II. Lying with two pillows in small of back	124	80	44
III. Standing	128	78	50
IV. Standing with one leg raised at right angles to trunk	126	76	50

DISCUSSION OF BLOOD-PRESSURE RESULTS. The above results confirm Erlanger and Hooker's finding of the remarkable decrease in pulse-pressure which is present when cases of orthostatic albuminuria assume the upright position. The point of special interest to us has been the production of almost as low a pulse-pressure when they are in the horizontal position with exaggerated lordosis artificially produced by placing two pillows in the small of the back. We do not understand why that is true unless the increased lordosis acts in some way through the sympathetic system. The fact that the maximum pressure remains practically constant in all the cases, the alteration taking place in the minimum pressure, is important. Invariably the albuminuria varied inversely as the pulse-pressure, being most marked in Case 1, which had a standing pulse-pressure of only 14. In this case there was no albuminuria when lying in bed, while with standing the output was about 2 gm. per liter, depending somewhat upon the degree of oliguria. In Case 4 the maximum albuminuria was 1.5 gm. per liter when standing, with its complete disappearance when lying flat in bed. Cases 3, 4 and 5 all showed moderate amounts of albuminuria when lying in the horizontal position, with two pillows in the small of the back. In Cases 1 and 2 this point was not determined.

In the 3 cases of acute nephritis examined the reduction in pulse-pressure is practically as marked as in the orthostatic cases, but in 2 of them there is a reduction in the systolic pressure. All 3 of these cases showed an albuminuria which varied inversely as the pulse-pressure. The remaining cases present more normal findings: that is, a slight reduction in pulse-pressure upon assuming the upright position, with the alterations taking place in either the maximum or minimum pressures, or in both.

KIDNEY FUNCTION. *The Nephritic Test-meal.* Nephritic test-meals, according to Mosenthal's¹⁹ modification of Hedinger and

¹⁹ Arch. Int. Med., 1915, xvi, 733.

Schlayer's²⁰ technic, were carried out in all 5 cases when in the recumbent and in the erect positions. In the latter the patient remained standing from 8 A.M. to 8 P.M. The results are typical, showing the marked oliguria with high concentration which takes place when in the upright position in contrast to a normal function when lying in bed. Neither by day nor by night was there any evidence of an inability to concentrate salt or nitrogen. Below two typical meals are given in full, one in each position:

NEPHRITIC TEST-MEAL.

Serial No. 1. September 9, 1916.

Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride.		Nitrogen.	
			Per cent.	Gm.	Per cent.	Gm.
8 to 10	26	1035				
10 to 12	30	1033				
12 to 2	41	1035				
2 to 4	51	1035				
4 to 6	40	1036				
6 to 8	55	1036				
Total day	243	0.925	2.20	1.90	4.56
Night, 8 to 8	200	1033	0.940	1.88	2.09	4.18
Total, 24 hours	443	4.08	8.74
Intake	1560	8.0	13.0
Balance	+1117	+3.92	+4.26

NOTE.—Standing from 8.00 A.M. until 8.00 P.M.

Serial No. 5. April 26, 1917.

Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride.		Nitrogen.	
			Per cent.	Gm.	Per cent.	Gm.
8 to 10	395	1011				
10 to 12	162	1024				
12 to 2	285	1018				
2 to 4	192	1019				
4 to 6	128	1023				
6 to 8	184	1019				
Total day	1346	0.675	8.97	0.508	6.80
Night, 8 to 8	370	1026	0.606	2.22	1.099	4.06
Total, 24 hours	1716	11.19	10.86
Intake	1760	8.5	13.4
Balance	+44	-2.69	+2.54

NOTE.—In bed all day.

THE RATE OF EXCRETION OF UREA AND OF CHLORIDES. Observations were also carried out as regards the kidney ability to excrete urea and chlorides when in the two positions. The findings are summarized in the following table:

²⁰ Deutsch. Arch. f. klin. Med., 1914, cxiv, 120.

THE RATE OF EXCRETION OF UREA AND OF CHLORIDES.

Serial No.	Date.	Position.	Weight, kilos.	Urine per 24 hours, c.c.	Urea.			Sodium chloride.					Thresh- hold.		
					Gm. per liter of blood. Ur.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	McLean's index.	Ambard K.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	Gm. per liter of plasma.			
												Calcu- lated.		Actual.	Differ- ence.
1	Oct. 29, 1916	Lying	40.2	9960	0.180	1.42	14.13	116	0.074	1.57	15.62	5.959	6.30	+0.341	5.961
	Oct. 30, 1916	Standing	40.2	1392	0.210	7.83	10.89	155	0.064	2.11	2.93	5.778	6.180	+0.402	6.002
2	Oct. 25, 1916	Lying	48.2	3259	0.270	6.78	22.08	146	0.066	3.14	10.20	5.918	5.980	+0.062	5.682
	Oct. 26, 1916	Standing	48.2	3216	0.180	6.91	22.22	337	0.044	3.74	12.02	5.958	5.800	-0.158	5.402
3	Mar. 20, 1917	Lying	41.48	3744	0.165	3.22	12.07	173	0.061	2.5	9.36	5.911	6.00	+0.089	5.709
	Mar. 24, 1917	Standing	41.8	1142	0.195	11.82	14.06	279	0.048	2.75	3.27	5.795	6.437	+0.642	6.262
4	Apr. 30, 1917	Lying	61.25	1512	0.255	16.95	25.61	237	0.052	13.2	19.96	6.148	6.062	-0.086	5.534
	May 1, 1917	Standing	61.25	864	0.255	23.01	19.87	214	0.055	14.2	12.27	6.042	6.094	+0.052	5.672
5	Apr. 24, 1917	Lying	52.6	2976	0.255	8.64	25.7	199	0.057	4.06	12.08	5.951	5.965	+0.014	5.634
	Apr. 25, 1917	Standing	52.6	1032	0.225	18.55	19.14	279	0.048	3.66	3.77	5.800	6.200	+0.400	6.020

Discussion of Excretion of Urea and of Chlorides. Four of the 5 cases show a hypersensitive condition of the kidneys when the upright position is assumed in that the rate of excretion of urea is increased. This is clearly demonstrated by the raised McLean's index and lowered Ambard constant. This increased rate of excretion fails to vary directly as the pulse-pressure changes.

The relation of the chloride threshold to the position and pulse-pressure is also most interesting. Four of the cases show a considerably raised threshold when in the upright position. We consider this to be a further indication of irritability.

The Phthalein Test. Phenolsulphonephthalein tests were performed upon 4 of the cases while in the recumbent and erect postures. The results are inconclusive, as 2 of the cases show higher rates of excretion when standing than when lying. The observations of Barker and Smith,²¹ as well as those of Hempelman²² also fail to establish any definite facts in this particular. Hempelman's observation that the most marked decrease takes place in the first hour is not confirmed by our results.

Findings. 6 mg. phthalein intramuscularly in lumbar region.

Serial No.	Position.	First hour.	Second hour.	Total.
1	Lying	61	21	82
	Standing	51	22	73
2	Lying	52	10	62
	Standing	76	18	94
4	Lying	70	26	96
	Standing	70	16	86
5	Lying	64	23	87
	Standing	75	17	92

PROGNOSIS. As regards the prognosis in these patients there is considerable difference of opinion, but the general consensus seems to be that with an improvement in their general tone and muscular development the condition will spontaneously disappear in later life. There is little danger that a true nephritis will develop if it has been excluded at first. Senator²³ believes that most cases can be traced to a low-grade inflammatory involvement of the kidneys, and for that reason he gives a doubtful prognosis. Heubner²⁴ has reported 1 case that came to a postmortem examination, the cause of death being cerebral embolism. On examination the kidneys were normal.

TREATMENT. Treatment has not been very satisfactory in most cases. Jchle used spinal and abdominal supports, which relieved the lordosis, with considerable satisfaction. Exercises which increase the muscular tone, especially that of the lumbar muscles, has proved beneficial in other cases. Working upon the theory that the albu-

²¹ AM. JOUR. MED. SC., 1916, cli, 44.

²² Am. Jour. Dis. Child., 1915, x, 418.

²³ Monographic Medicine, i, p, 413.

²⁴ Berl. klin. Wehnschr., 1907, xlv, 1.

minuria was associated with a diminished coagulability of the blood, Wright and Ross²⁵ treated a few cases with calcium, for which they claimed favorable results. One of our cases (Serial No. 1) we treated by a spinal brace, with an abdominal support, with a complete disappearance of the albuminuria and a marked improvement in his general condition.

CONCLUSIONS. In considering our findings we believe that the condition of orthostatic albuminuria is a general systemic disturbance, manifesting itself in faulty development, as shown by a general visceroptosis, a "drop heart," a generalized muscular and visceral atonia, which we know to be associated with varying degrees of vasomotor instability. The symptoms so commonly complained of, such as headache, lassitude, constipation and loss of weight, are the natural results of physical conditions. The increased lordosis that is usually present we consider to be a symptom due to the faulty muscular development and tone of the lumbar muscles. This exaggerated lordosis is well recognized in many muscular dystrophies and atrophies and in other conditions involving the lumbar and abdominal muscles. The low pulse-pressure is undoubtedly the cause of the albuminuria rather than a mechanical interference with the venous return from the kidneys. To us it is an exceedingly interesting fact that the pulse-pressure can be lowered to almost the same degree by artificially producing lordosis while in the horizontal position as when erect. The albuminuria in all our work varied inversely as the pulse-pressure, regardless of the position.

**STUDIES IN FRACTIONAL ESTIMATION OF STOMACH
CONTENTS. III. EFFECTS OF HYDROCHLORIC ACID
THERAPY ON THE ACID TITER OF THE
STOMACH DURING DIGESTION.¹**

BY BURRILL B. CROHN, M.D.,

ASSISTANT IN PHYSIOLOGICAL CHEMISTRY, PATHOLOGICAL LABORATORY, MT. SINAI
HOSPITAL, AND FIRST ASSISTANT, DEPARTMENT OF GASTRO-ENTEROLOGY,
MT. SINAI HOSPITAL DISPENSARY, NEW YORK CITY.

(From the First and Second Medical Services and the Pathological Laboratory of the
Mt. Sinai Hospital, New York City.)

IN previous articles by the author² the method of fractional estimation of stomach contents was chosen as a means of studying the direct effect of alkalis upon gastric digestion. The mode of

²⁵ Lancet, 1905, ii, 1164.

¹ This study was carried out under the grant of a George Blumenthal, Jr., Fellowship in Pathology.

² Crohn and Reiss: AM. JOUR. MED. SC., 1917, cliv, 857; Crohn: AM. JOUR. MED. SC., 1918 clv, 801.

activity of antacid substances was studied and their effect upon the secretion of acid, emptying time of the stomach, the regurgitation of biliary contents, etc., were noted.

In this communication, using the same methods, the subject of hydrochloric acid medication will be discussed, that is, the results following the therapeutic administration of acid will be correlated and conclusions drawn as to the best method for the administration of this commonly employed medicinal agent.

There is to some extent the same degree of confusion and the same lack of unanimity of opinion in the field of acid therapy as was observed in the previous discussion of the use of the antacids. One finds in the literature only scant reference to the dosage of acids to be given in such conditions as achylia gastrica, anacidity, chronic gastritis, etc. No uniform method of administration has been adopted either as regards the amount, the proper time of administration or the frequency of repetition. Nor does the literature afford an instance of an attempt to study scientifically the effect produced in the human digesting stomach by the introduction of acid. Cushny³ speaks of the dose as 5 to 30 minims of the dilute hydrochloric acid of the United States Pharmacopœia; he implies that the dose is to be administered once only. Leo⁴ published the most exhaustive study of the effects of HCl administration in man. He utilized relatively large doses of hydrochloric acid⁵ corresponding to from 75 to 225 minims of dilute muriatic acid of the United States Pharmacopœia. By withdrawing the stomach contents during digestion he was able to demonstrate some increase in the acid titer of the chyme. Yet in spite of the often very large dosage employed in his simple therapeutic experiments free acid was rarely demonstrable in the gastric contents. The free and total acid content of the specimens withdrawn during the tests were never seen to approach even that of a normal individual. In the experiments of Leo single doses were utilized; he summarizes his remarks by urging a single administration of 15 to 60 minims of our dilute muriatic acid as the proper dose to an adult.

Boas⁶ accepts the views of Leo without criticism and without adding any suggestions drawn from his vast experience as a clinician. Ortner⁷ takes the stand that it is impossible to administer hydrochloric acid in sufficient amounts to leave some free acid in the stomach as found under normal conditions. He advises therefore the administration of the dilute muriatic acid in doses of 10 to

³ Pharmacology and Therapeutics, 1903, 3d ed., p. 565.

⁴ Die Salzsäuretherapie auf Theoretische und Praktischer Grundlage, Berlin, 1908.

⁵ The hydrochloric acid of the German Pharmacopœia contains 25 per cent. of the acid by weight, that of the United States Pharmacopœia only 10 per cent.; the necessary correction must therefore be made in reading all figures from the German literature.

⁶ Diagnostik und Therapie der Magenkrankheiten, 6th ed., p. 350.

⁷ Treatment of Internal Diseases, 1908, translation, 4th ed., p. 415.

30 minims, repeated every half-hour, until digestion is complete. Bourget⁸ recommends that acid be administered as a 2 per cent. solution of hydrochloric acid and gives 100 to 200 c.c. distributed during the period of digestion.

In the absence of a uniform method for the administration of acid therapeutically it appeared advisable to the author to undertake a study of the effects of acid upon the stomach during digestion. Particular reference was paid to the changes in acid titer of the chyme both directly after the taking of the acid and during the subsequent cycle of digestive activity.

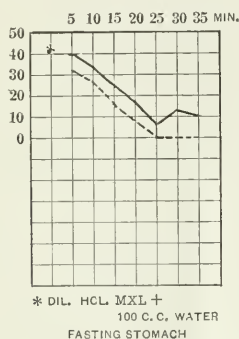


FIG. 1

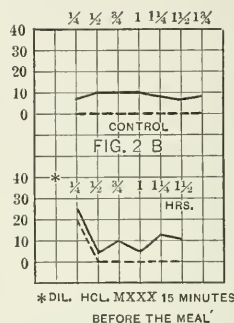


FIG. 2

METHOD. The fractional method of obtaining stomach contents, was utilized in this study. The technic was identical with that employed in the previous study⁹ on antacid activities. Oatmeal gruel was used as a test breakfast. Specimens were withdrawn every fifteen minutes and the material so obtained was examined quantitatively for free and total acid, presence of ferments, etc. In each case a control curve was obtained on the first day of the experiment; this afforded a basis for the comparison with the result on subsequent days when acid was administered.

EFFECT OF ADMINISTRATION OF HYDROCHLORIC ACID IN SINGLE DOSE. In order to study the effect of a single dose of acid, cases of achylia gastrica or cases of pernicious anemia, with complete anacidity, were chosen. These cases were all uniform in presenting in the control fractional estimation tests a complete absence of free acid throughout digestion. The total acidity ranged usually between 6 and 10 per cent. per 100 c.c., occasionally reaching as high as 16 per cent.

For the sake of brevity and clarity the experiments are described in the briefest style, thus allowing the reader easily to grasp the

⁸ Die Krankheiten des Magens und Ihre Behandlung, first ed., p. 94.

⁹ Crohn and Reiss and Crohn: AM. JOUR. MED. SC. (in press).

effect of the acid administered under the varying condition. While the individual experiments quoted appear as single experiments, most of them are simply illustrative examples of a group of duplicate attempts to ascertain the result of one method of administering the acid therapeutically.

Experiment 1. Patient suffering from pernicious anemia; gastric analysis: achylia gastrica. Dosage, 40 minims dilute HCl, United States Pharmacopœia, diluted with 100 c.c. of water. The medication was administered after the fasting stomach had been emptied by aspiration. No test-meal was given in this experiment.

Results (Fig. 1). Directly after the administration of the dose the total acid was 40 per cent., the free acid 32 per cent.¹⁰ Titration of successive specimens withdrawn at five-minute intervals showed a rapidly diminishing acid titer. At the end of twenty-five minutes

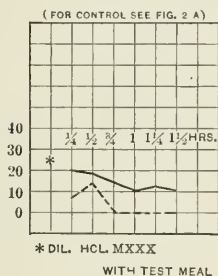


FIG. 3

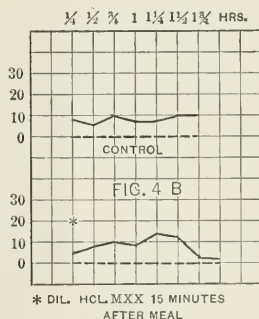


FIG. 4

the titration was identical with that of the fasting residue before the administration of the acid. Free acid was again absent; total acid was not above 10 per cent. In the specimens withdrawn, in twenty, twenty-five and thirty minutes after giving the acid abundant mucus was present.

Conclusions. Hydrochloric acid administered therapeutically to the fasting stomach promptly disappears from that organ, the last trace leaving within twenty-five minutes.

(Experiments 2 to 5 were performed upon various cases of achylia gastrica.)

Experiment 2. Dilute HCl, 30 minims administered fifteen minutes before the usual test-meal of oatmeal gruel¹¹ (Fig. 2). It was noted that directly after swallowing the gruel the titration of the chyme showed a free and total acidity of 20 per cent. and 24

¹⁰ The acid titer of the gastric contents is expressed throughout in cubic centimeters of decinormal sodium hydrate required to neutralize 100 c.c. of the chyme examined.

¹¹ The dose of dilute HCl was always administered in 100 c.c. of water.

per cent. respectively. At the next titration, fifteen minutes later, free acid had disappeared and total acid was only 4 per cent. During the remainder of the observation period the curve was identical with that of the control experiment in which no acid was administered.

Conclusions. The administration of acid before a meal exerted no influence on the acid secretion of the subsequent digestive cycle.

Experiment 3. Dilute HCl, 30 minims administered with the test gruel (Fig. 3).

Result. A slight increase of acidity was noted during the first half-hour of digestion. The maximal total acidity was 20 per cent. Thereafter a return to the level of the control curve was noted. Free acid was present during the first half-hour only; during this time increasing amounts of mucus were observed.

Conclusions. The therapeutic administration of acid with a test-meal is of advantage only for the first half-hour; the increase in the acid titer of the chyme is moderate in degree.

Experiment 4. Administration of dilute HCl, twenty minims, fifteen minutes after the test-meal (Fig. 4).

Result. A complete failure to relieve the condition of anacidity was noted. At no time after the administration of the therapeutic acid was free acid demonstrable in the gastric contents. The curve of gastric acidity (total acidity) seemed slightly elevated in the experiment. However, on comparing the average acidity of the experiment with that of the control test no increase in the total acidity was observable.

Conclusion. Twenty minims of dilute hydrochloric acid failed to improve the condition of anacidity when given with a test-meal.

Experiment 5. The conditions were the same as in Experiment 4 except that the dose of the acid was double—that is, forty minims of acid were given fifteen minutes after the test gruel was taken. This experiment was repeated under identical conditions upon three different patients, all suffering from achylia gastrica.

Results. With the larger dose employed in these experiments more favorable results were observed (Figs. 5 and 6). The increase in acidity was observed and was limited to only the first hour after the administration of the therapeutic acid. Thereafter the curve was identical with that of the control observation. The maximal increase of acidity took place in 2 of the cases directly after the taking of the medication; in the third case the maximal rise of acidity was noted one hour after the acid was taken. Following the maximal rise in acid titer there was a gradual return to the condition of anacidity. The highest titer of total acid was 54 per cent., 30 per cent. and 22 per cent. respectively in the 3 cases.

Conclusions. Forty minims of dilute HCl gave a definite though moderate increase of acidity; this increase was temporary in dura-

tion, being usually limited to the short period directly after taking the medication.

(Experiments 6 and 7 were performed upon cases of functional subacidity.)

Experiment 6. Ten c.c. of decinormal HCl were administered to a patient one and a half hours after the ingestion of the usual test-meal. This dose corresponds roughly to 5 minims of the dilute HCl of the United States Pharmacopœia.

Result. No effect was seen upon the course of the acid curve.

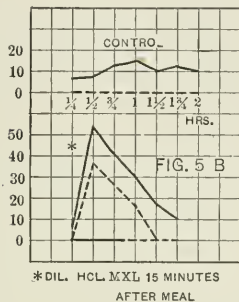


FIG. 5

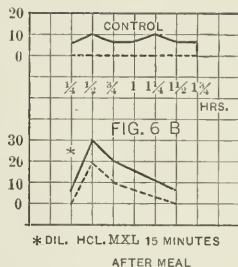


FIG. 6

Experiment 7. 50 c.c. of decinormal HCl (corresponding to 25 minims of dilute HCl) were administered three-quarters of an hour after the usual test gruel was ingested.

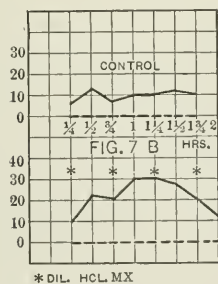


FIG. 7

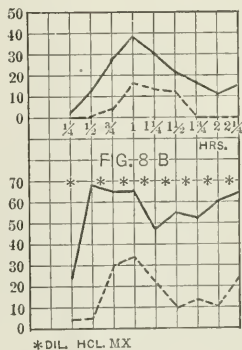


FIG. 8

Result. A slight increase in both free and total acidities was noted, the increase being sustained to the end of digestion. The increase in total acidity was from 54 per cent. in the control to 68 per cent. in the case under experimentation.

(Experiments 8 and 9 consisted of the administration of repeated small doses of dilute HCl at frequent intervals during digestion.)

Experiment 8. To a case of an acidity, dilute HCl, 10 minims were administered every half-hour during digestion (Fig. 7).

Result. A definite increase in acidity was observed throughout the digestive cycle. While the increase in total acidity was not marked (maximum total acidity was 30 per cent.), yet this increase was sustained for one and three-quarter hours. As the digestive cycle approached its conclusion even the administration of the therapeutic acid was unable to maintain an acidity of over 14 per cent. Free acid was absent in both the control and the experimental case. Motility was slightly accelerated.

Conclusions. Ten minims of dilute HCl administered every half-hour was a mild though efficient method of increasing total acidity during digestion. It was, however, insufficient to produce free acid at any time in the cycle of digestion.

Experiment 9. This experiment consisted of the administration of 10 minims of dilute HCl every fifteen minutes during digestion (Fig. 8).

Result. A definite and noteworthy improvement in the average titration of total acidity was observed. While in the control curve the maximum point reached was 38 per cent., during the experimental exhibition of the acid a maximum acid titer of 68 per cent. was attained and was maintained, with slight variations only, throughout the digestive cycle. The average total acidity in the control curve was 20 per cent.; after the administration of the acid it was 55 per cent. The motility of the stomach was unchanged during the experiment, emptying taking place under both conditions in two and a quarter hours.

DISCUSSION. The above experiments were performed with the idea of simulating, so far as possible, the clinical custom of administering hydrochloric acid to patients suffering from conditions of diminished or absent gastric secretion. Before proceeding to note the effects of acid administered during or after a meal one must have a clear concept of the consequences of administering hydrochloric acid alone to the fasting stomach. Experiment 1 demonstrated that a comparatively large dose of HCl (diluted with 100 c.c. of water) when taken by a fasting person suffering from achylia gastrica creates a temporary acidity up to 40 per cent. (0.146 per cent.). This acidity rapidly diminishes and is no longer to be demonstrated twenty-five minutes later. What has happened within the stomach during this time? The most striking fact is the rapid disappearance of the acid which has been given. Evidently the stomach quickly expels the acid liquid through the pylorus, consuming the same time that it takes to empty an equal amount of distilled water. The second fact is that the titer which immediately results upon the introduction of the acid is not maintained but is rapidly neutralized or diluted. Thus, each succeeding titration shows a diminishing degree of acidity. The agencies employed in this neutralization

are two: The primary one is a secretion of a watery gastric juice containing no acid ions; this hydrorrhea progressively dilutes the acid which is introduced. The second agency is a secretion of alkaline mucus such as is characteristic of the pyloric region of the organ; this process is evidenced by the rapidly increasing amounts of mucus seen to be precipitated in the progressive specimens.

The actual course of the neutralization is to be noted in the following statement:

Titer of therapeutic acid upon introduction, 0.244 per cent.

Titer of chyme five minutes after introduction, 0.146 per cent.

Titer of chyme ten minutes after introduction, 0.124 per cent.

Titer of chyme fifteen minutes after introduction, 0.0876 per cent.

Titer of chyme twenty minutes after introduction, 0.065 per cent.

Titer of chyme twenty-five minutes after introduction, 0.022 per cent.

That the process of dilution and neutralization ceases upon the disappearance of the last trace of free acid is proved by the fact that immediately thereafter no material is attainable upon aspiration. At no time is a secondary rise of acid to be noted. The attempt to stimulate the production of gastrogenous acid by the introduction of an acid substance fails.

The results of these experiments corroborate those of Spencer, Meyer, Rehfuß and Hawk,¹² who similiarly introduced large quantities of hydrochloric acid into the stomach of *normal* individuals. They observed a rapid emptying of the acid associated with a progressive neutralization of the excess of acid introduced. In their experiments they employed acid solutions of much greater concentration (0.542 per cent. and 0.4 per cent.), yet the normal titer of the gastric contents was resumed within one hour. The rate of expulsion and of neutralization is approximately proportionate to the amount and concentration of acid introduced.

In my series of experiments numbered 2 to 5 inclusive, dealing with cases of achylia, the acid was administered coincident with or soon after the taking of the test gruel. The action of the acid, when so given, is in no way different from that when taken upon a fasting stomach. It is seen that the diminution of acid titer is progressive; the evacuation of the excess of acid takes place in from half to one hour, depending upon the amount and concentration of acid introduced. Thus it was observed that whether 30 minims of dilute acid were given fifteen minutes before or given directly after the swallowing of the test gruel the process of neutralization and expulsion was identical; that is, one-half an hour after the time of giving no further beneficial effect of the acid was noticeable.

The fourth experiment demonstrated that 20 minims of HCl

¹² Am. Jour. Physiol., 1915, xxxix, 457.

when given as a single dose is insufficient to effect a rise of acid titer in the digesting stomach of a case of achylia gastrica. Doubling the dose (40 minims) is much more effectual, though again the result is purely temporary. Any increase in acid titer was directly ascribable to the mineral acid added as part of the experiment; a secondary physiological stimulation of the gastric mucosa characteristic of "human acid secretion" was never demonstrable. It must not be forgotten that these experiments were not performed on normal individuals but on persons suffering from abnormal conditions. However, it is only in persons so diseased that the indication for acid therapy exists.

Experiments 6 and 7 consisted of the introduction of small doses of HCl in cases of subacidity. Insofar as an increase in the acid titer was observed the results were practically *nil*.

The foregoing experiments demonstrated that a single dose of acid, no matter how large (5, 10, 15, 20, 25, 30 or 40 minims), had failed to produce a rise of acidity which satisfied the clinical requirements—that is, created a sustained rise in acidity during the period of active digestion. Therefore, Experiments 8 and 9 were performed to ascertain the effects of small but repeated doses upon the titer of the digesting meal. Thus in Experiment 8 the aggregate dose of 40 minims was divided into four portions and 10 minims were administered every half-hour. Small as the individual dose was the method of giving repeated doses was successful in that the typical curve of achylia was transformed into that of a case of subacidity. The dosage and method of administration were insufficient to produce at any time free hydrochloric acid in the digesting fluid; however, a partial success was achieved insofar as a total acidity between 20 and 30 per cent. was maintained throughout the greater part of the digestive cycle.

In Experiment 9 the same method of administration was continued except that the individual doses followed each other at more frequent intervals. The resultant effect was proportionately better. The fractional curve of a case of marked subacidity was converted into that of a normal or isosecretory curve; the increased acidity was maintained at that level throughout the course of digestion.

It must be conceded that the method of administering repeated small doses of acid at frequent intervals is hardly a practical one for every-day clinical use. Where it is possible, however, the method should be adopted. For temporary usage it is often highly satisfactory.

To the clinician who is anxious to reproduce the conditions of a normal digesting stomach in a case of achylia or marked subacidity the following conclusions may be offered from these experiments:

1. The customary method of administering hydrochloric acid as a single dose is, in most instances, insufficient to relieve the abnormal condition.

2. Small single doses (5 to 20 minims dilute HCl, United States Pharmacopœia) fail completely. Larger doses (25 to 40 minims) give better results, though the effects are but temporary, lasting usually for the first half-hour only after administration.

3. The method of administering small doses at frequent intervals, that is, every half- or better every quarter-hour, is a more efficient one for accomplishing the desired effect.

4. The custom of giving acid before a meal has no advantages. The best results are seen when it is taken during the early part of the digestive cycle.

5. The effect of acid so administered is purely a local chemical one. A resultant physiological stimulation of the mucosa was never demonstrable from the experiments.

AUTOSEROTHERAPY IN TUBERCULOUS PLEURISY, WITH EFFUSION.

BY J. CURTIS LYTER, M.D.,

INSTRUCTOR IN INTERNAL MEDICINE, ST. LOUIS UNIVERSITY MEDICAL SCHOOL;
VISITING PHYSICIAN, ST. LOUIS CITY HOSPITAL, ST. LOUIS.

IN the year 1894 Gilbert reported before the International Medical Congress at Rome a series of cases of serofibrinous pleurisy which he had treated by withdrawing a few cubic centimeters of the fluid from the chest and immediately injecting it into the subcutaneous tissues of the patient. This treatment, designated by Gilbert "autoserotherapy," was said by him to be highly efficacious in promoting a rapid absorption of the effusion, and following the absorption to leave the patient in good general condition.

A number of years later this investigation was reopened by a number of European clinicians and in more recent years in America as well. A vast majority of the investigators, after observation of a varying number of cases, conclude that autoserotherapy not only promotes a rapid absorption of the pleural exudate in most cases, but also prevents to no small degree the formation of dense, fibrous adhesions so frequently seen subsequent to pleural effusions. Fedde, Tchigayoff, Marcou, Geronzi, Durand and Weil are among the European clinicians to report very favorably upon the results obtained by this method of treating pleural effusions. Fishberg,¹ after reviewing the literature most diligently, reported 14 cases of tuberculous pleural effusions treated by autoserotherapy, with immediate absorption in 12 of the cases. Fishberg concludes that since the method is without danger, and in view of the very favorable results obtained, it should be more generally employed. He

¹ Jour. Am. Med. Assn., March 22, 1913, No. 12, vol. lx.

also states that autoserotherapy is successful in some cases in which puncture and aspiration fail. All this would seem to indicate that in a certain number of cases this form of treatment should be instituted.

Following the reports so favorable by the above-mentioned and other clinicians a discussion ensued as to why the injection of the fluid caused this absorption. As yet there is no uniformity of opinion as to what substance in the effusion when injected subcutaneously is capable of thus promoting this absorption. Gilbert explained the result as due to tubercle toxins within the effusion, and for a time this view was generally accepted. Zimmerman² considers that he has definitely proved that the absorption is caused by the presence in the effusion of an autolytic substance, the product of cell metabolism. Zimmerman also states that the injection of this fluid produces a leukocytosis similar to that produced by the injection of a foreign proteid. George Eisner³ after considerable experimental work upon rabbits and guinea-pigs, producing a pleural effusion in rabbits by the injection of the old oil of turpentine into the pleural cavity and very ingeniously producing tuberculous effusions in guinea-pigs, concludes that the injection produces a leukocytosis and an absorption of the effusion. He believes that the presence of specific bodies in the exudate accounts for its efficacy in promoting absorption.

After a careful study of the physical elements involved in the absorption of effusions one might be inclined to question the reliability of the observations of those reporting such wonderful results from a method the physiological aspects of which are not even definitely suspected. In fact, Hochhaus, Ansperger, Szureck and others have produced evidence satisfactory to themselves that about 80 per cent. of all tuberculous effusions undergo spontaneous absorption, and that as autoserotherapy is successful only in about the same percentage of cases its absolute dependability is very much open to question. It would seem that knowledge gained at the autopsy of cases dying with pleural effusions should serve us in some capacity in arriving at a conclusion as to whether or not the very nature of the effusion would inhibit its absorption no matter what method of stimulation was used. At these autopsies one observes not only the pleuræ covered by a thick, rather closely adherent layer of fibrin, but that throughout the effusion there are also large masses of fibrin unattached.

As this fibrinous coating of the pleura must become more or less organized before there are lymph and blood capillaries sufficiently in contact with the effusion to permit the absorption by them, any treatment to promote absorption previous to this organization must meet with failure. Likewise, no spontaneous absorption can occur

² Cited by Fishberg.

³ Cited by Fishberg.

previous to this organization. When once the organization is complete the absorption of the effusion spontaneously is the natural phenomenon. Any method of treatment at this stage will be accompanied by good results. Without question there are cases of tuberculous effusion which undergo spontaneous absorption after but a few days' existence, the absorption meeting no inhibition because of the small fibrin content of the fluid, consequently the usual time of organization not being required. These cases resemble very closely ordinary transudates in the facility with which absorption is promoted.

In numerous instances, unless conducted under extremely careful observations, clinical results are very prone to cause erroneous impressions and the interpretations of these impressions lead to inconclusive reports. In consideration of the condition under discussion, errors of observation could be very numerous because of the several factors influencing absorption, namely, the character of the effusion, especially as to its fibrin content, the duration of the effusion bearing more specifically upon the organization of the fibrin coating of the two pleural surfaces and the general constitutional condition of the patient, and more especially the condition of the pleura previous to the time of the effusion. When there existed a previous extensive pachypleuritis, absorption of the effusion could scarcely be expected because of the paucity of lymph and blood capillaries. Observing these factors, one can note that the absorption could either occur very early in the course of the effusion or at some later period; also, that when the conditions for the absorption were perfected the absorption in most cases would be very rapid.

In consideration of the physical elements involved in the absorption of fluids from natural body cavities in general we might recall that absorption must occur through the blood and lymph channels regardless as to whether the fluids be a transudate or an exudate. This being borne in mind we would expect the methods employed to cause absorption of transudates to yield equally as good results toward causing the absorption of exudates were it not for the difference in the physical characters, especially as to their fibrin content, of these two entirely different fluids.

Clinical experience has long taught that free purgation causing watery evacuations will cause a rapid absorption of transudates in many cases, and that in no case of tuberculous exudate would we expect results from this form of treatment. Since the blood and lymph capillaries must be a constant factor in the two conditions, we must explain the difference in their absorbability only upon the known physical differences of the two fluids. The tuberculous exudate being rich in fibrin and albumin would not only occlude the blood and lymph capillaries but further embarrass absorption by this content. If this reasoning is true it follows that any form of

treatment administered to promote absorption of a tuberculous effusion must be given with the intention of either changing the physical character of the fluid, thus rendering it the more absorbable, or to stimulate the capillaries in such a way as to render them more capable of absorbing the exudate more rapidly than is the rule in the untreated cases. Since the pleural surfaces in which the absorbing capillaries are situated are, as a rule, densely covered by fibrin deposits through which fluid could hardly be expected to pass until organization of the fibrin had occurred, it seems quite impossible for any form of treatment to be of any value from this stand-point; likewise, it is scarcely logical to suppose that any form of treatment could so change the physical characters of the exudate as to render it more absorbable.

Since the year 1911 I have treated 23 cases of tuberculous pleural effusion by Gilbert's method. The needle of an aspirating syringe of 10 c.c. capacity was placed in the chest and 5 c.c. of the effusion drawn into the syringe. The needle was then withdrawn until the point was immediately beneath the skin, when the needle was introduced deeply into the subcutaneous tissue and the patient received the entire 5 c.c. subcutaneously. The treatment was administered every second day until six injections were given unless the fluid was absorbed before the last injection was due. The patient was watched daily to see if any change could be noted in the level of the fluid. In many of these cases the fluid was observed under the fluoroscope weekly for several weeks following the treatment, consequently the results to be recorded represent the full effect of the treatment.

The twenty-four-hour quantity of urine, with its specific gravity and indican content, was accurately kept for one or two days previous to the administration of the treatment and throughout the time of the treatment. The diet and liquid intake were kept at a definite quantity and character during the entire investigation. The leukocytes were counted before each injection and in most cases twice during the twenty-four hours following each injection. The temperature, pulse, and respiration were charted regularly during the entire treatment. An analysis of these 23 cases reveals the following results:

Eight cases of the series underwent complete absorption within two weeks of the beginning of the treatment. Of these 3 revealed absorption by the sixth, 1 by the eighth, 1 by the tenth, 1 by the twelfth and 1 by the fourteenth day. Of these 8 patients only 2 had a rise in temperature which could in any way be attributed to the injection. Of these 2 patients 1 revealed marked diaphoresis while the other revealed both diaphoresis and diuresis. Of the remaining 6, 1 had marked diuresis, the urine increasing 800 c.c. during the first twenty-four hours following the first treatment, but there was no diaphoresis. The other 5 of the 8 revealed neither rise in temperature, diaphoresis nor diuresis. In no instance was there a

notable increase in the leukocytes following the injection. The greatest increase in any case was in 1 case in which the leukocyte count rose from 12,400 to 13,800. This could quite easily be due to error in counting. In none of the cases was there any increase in the urinary indican, as one would expect were there an autolytic enzyme at work causing the absorption.

Of the 15 unsuccessful cases each patient received 5 c.c. of the fluid every second day for twelve days. Six of these were under observation for two weeks following the last injection, 5 were observed for four weeks, 2 for eight weeks and 2 for twelve weeks following the last injection. No change was noted in the general condition of the patient or in the amount of fluid present in 4 of those observed for two weeks following the injection; 2 of this series died within the two weeks following the last injection, 1 death being attributed to cardiac and 1 to respiratory failure. Of the 5 who were observed for a period of four weeks after the treatment was administered no case revealed any change either in the general condition or in the amount of fluid present. The same is true of the 2 cases observed for eight weeks following the treatment. Both of the cases observed for three months following the treatment died at the end of the three months with a rapidly progressing pulmonary tuberculosis, 1 with extensive cavity formation. The clinical impression in these 2 cases was a rapid progression following the treatment of a previous perfectly stationary tuberculosis. In none of these 15 unsuccessful cases was there an increase in the leukocytes following any of the injections, neither was there diuresis noted upon a carefully taken twenty-four-hour quantity of urine. What diaphoresis or elevation of temperature occurred following the injection in any of the cases could more logically be explained by the tuberculosis itself. In no case was there any definite increase in the urinary indican.

The results obtained in this series of cases is opposed to those recorded by Fedde, Tchigayoff, Marcou, Geronzi, Durand, Weil and Fishberg. These investigators report varying numbers of cases in which an immediate absorption is produced in approximately 80 per cent. In our series there were 8 absorptions occurring out of 23, or 34 per cent. The absorption in these 8 was more probably due to the natural physical phenomena than to the stimulating effect of the treatment. Our results indicate not only that the treatment does not cause absorption, accompanied by diuresis, diaphoresis, rise of temperature and leukocytosis, but that in some cases it is not entirely devoid of deleterious effects upon the tuberculous process in the lung. The assertion that 80 per cent. of all tuberculous effusions undergo spontaneous absorption should be qualified, as the spontaneous absorption may not occur for months, depending most probably upon the organization of the fibrinous covering of the pleura.

**RELATION OF HOUSING TO PULMONARY TUBERCULOSIS:
REPORT ON 36,062 CASES.¹**

BY FRANK F. D. RECKORD, M.D.,

DEPUTY MEDICAL INSPECTOR OF TUBERCULOSIS DISPENSARIES, PENNSYLVANIA
STATE DEPARTMENT OF HEALTH, HARRISBURG.

THE prevention of tuberculosis is far more important than its cure, consequently all those who are attacking tuberculosis in any of its phases should become sanitarians. There is an intimate association between good housing and economic progress. The essential prerequisites of efficient democracy is a healthful home-life, with elimination of all destructive elements now present in unsanitary homes and grounds and with positive presence of constructive elements: sanitation, ventilation, sunlight, space and privacy.

It has been reported that tuberculosis is a disease which, in the majority of cases, occurs in houses of 3 rooms and under; the number of cases is larger in 2-room houses than in 3, is larger in houses of 1 room than in 2, also the number of cases of tuberculosis and pneumonia increases almost in direct proportion to the number of small overcrowded houses in any district or ward of a city.

Some thirty years ago the first thoroughly systematic attempt was made by Dr. Russell, in Glasgow, to show a definite relation between the size of the house and the health of the occupants. These studies applied intensively in Glasgow, and to a certain extent statistically, in eight Scottish cities, established the fact that death-rates in 1-room dwellings were higher than in 2-room dwellings, that death-rates in 2-room dwellings were higher than in 3-room dwellings and that 3-room dwellings exceeded those of 4-room dwellings. These factors stood out independent of location of dwellings or surroundings. It is true, however, that unsanitary conditions were almost synonymous with small dwellings.

Later studies and conclusions of Dr. A. K. Chalmers, Health Officer of Glasgow, would indicate statistically if we use infant mortality as an index and indicate the death-rate of infants in 1-room apartment by the figures 100 that the 2-, 3- and 4-room apartments would be indicated by an index of 78, 61 and 49. In other words, the child born in the 1-room dwelling has only half as good a chance for its life as one born in a dwelling of 4 rooms or larger; the chance in a 3-room apartment against the one is as 61 to 100 and in the 2-room dwellings as 78 to 100, while with the death-rate from all diseases from the end of the first year to the end of the fifth year the relative rates are: for 1-room apartment 100, the 2-room apartment 74, the 3-room apartment 44 and the 4-room apartment and upward 25.

¹ Read before the Harrisburg Academy of Medicine, April 4, 1918.

It not only happens that the infant death-rate, that is, the rate of children under one year, is greatly increased in the 1-room apartment; but it is perhaps equally true that those who escape death are physically handicapped, so that in the next period or in the early years of life—that is, between the first and fifth year—they are much more likely to be sacrificed to other diseases. These facts are clearly brought out by the statistics of Dr. Chalmers, who shows that between the ages of one to five the death-rate per thousand for 1-room houses is 16.6, for 2-room apartments only 12.6, for 3-room apartment 7.2, for 4-room apartments and upward 3.1 per thousand.

In relation to tuberculosis, Dr. Chalmers reported that the overhead reduction during a decade was about 25 per cent., and this was fairly maintained in each class of house, save in four apartments and upward. He found that the female rate at all ages was higher than the male in houses of 1 and 2 apartments, and generally that in 1-apartment houses it was below the male rate only at the ages of twenty to twenty-five and forty-five to seventy-five and in 2-apartment houses at the ages of one to five, twenty to twenty-five and from forty-five upward. An excessive drift of male consumptives at these ages to parochial hospitals might tend somewhat to explain this excessive female incidence in houses, but there is no evidence of this in the institutional death-rate, which shows, indeed, a continuously excessive female rate at ages five to fifty-five save between ten and fifteen and again from twenty-five to thirty five.

In 3- and 4-room apartment houses the rate for males of all ages exceeds that of females. In 3-room apartment houses, however, the female rate exceeds the rate at ages under twenty, while in 4-room apartments the female excess occurs only at the period of five to ten and again over seventy-five. Applying the test of their standard population to these rates the association with the house appears to be quite definite.

* CALCULATED DEATHS IN UNIFORM POPULATION.

	Popula- tion.	One apartment.	Two apartments.	Three apartments.	Four apartments.	Institutions and shipping.
Males . . .	48,605	86	66	48	39	245
Females . . .	51,395	102	70	39	22	327
Death-rate	100,000	188	136	87	61	572

From the statistics which I have gathered together from the 116 Pennsylvania State Tuberculosis Dispensaries it is interesting to note in this connection the number of rooms per family and the number of persons in a family in a long series of cases and over a period of time that makes the information of value.

In a study of 36,062 families, covering a period of five years, it was found that 1192 families had one member or representing 1192 members:

2491	families had	2	members or representing	4,982	members.
4573	"	3	"	13,719	"
5767	"	4	"	23,068	"
6056	"	5	"	30,280	"
5487	"	6	"	32,922	"
3982	"	7	"	27,874	"
2849	"	8	"	22,792	"
2612	"	9	"	23,408	"
1053	"	10 or over	"	10,530	"

Thus the sum total represents 36,062 families and 190,767 members, or an average of 5.2 members per family.

Covering the same period of time and the same number of families—namely, 36,062—the number of rooms per family were found to be as follows:

4,025	families occupied	1	room or representing	4,025	rooms.
10,134	"	"	2 rooms	20,268	"
12,708	"	"	3 rooms	38,124	"
5,718	"	"	4 rooms	22,872	"
3,477	"	"	5 and over	17,385	"

The sum total of families, as above stated, is 36,062 and the number of rooms amounts to 102,674, making an average number of 2.8 rooms per family.

It is likewise interesting to note in connection with these 36,062 cases the number of persons in the family compared with the number of rooms occupied. I found that:

1109	cases having	1	member	to a family occupied	1	room.
989	"	"	2 members	"	"	1
777	"	"	3	"	"	1
508	"	"	4	"	"	1
330	"	"	5	"	"	1
168	"	"	6	"	"	1
77	"	"	7	"	"	1
34	"	"	8	"	"	1
33	"	"	9 and over	"	"	1

Total 4025 families composed of 1 up to 9 and over members occupied 1 room.

Just as astonishing is the data concerning the number of people that lived in 2 rooms:

48	families having	1	member	to a family occupied	2	rooms.
910	"	"	2 members	"	"	2
1740	"	"	3	"	"	2
2127	"	"	4	"	"	2
1859	"	"	5	"	"	2
1486	"	"	6	"	"	2
923	"	"	7	"	"	2
558	"	"	8	"	"	2
483	"	"	9	"	"	2

Thus 10,134 families composed of 1 up to 9 and over members were quartered in 2 rooms.

Continuing the study further, I found that 12,708 families made up of 1 to 9 and over members abode in 3 rooms as follows:

20 families having 1 member to a family occupied 3 rooms.									
415	"	"	2 members	"	"	3	"		
1423	"	"	3	"	"	3	"		
2113	"	"	4	"	"	3	"		
2485	"	"	5	"	"	3	"		
2295	"	"	6	"	"	3	"		
1673	"	"	7	"	"	3	"		
1112	"	"	8	"	"	3	"		
1172	"	"	9 and over	"	"	3	"		

From the above information it will be noted that 26,867 families out of the total 36,062 under consideration of 1 to 9 membership, or 74.5 per cent., occupied from 1 to 3 rooms.

Of the remaining 9195 families 5718, or 15.9 per cent., composed of the same number of members as given, occupied 4 rooms, while 3477 families, or 9+ per cent., lived in 5 rooms and over.

From this compilation of figures this interesting and striking summary is obtained:

Total number of rooms occupied by families of 36,062 patients, the number of whose rooms is given	102,674
Membership of families of 36,062 patients, 5.2 members to family	190,767
Average number of persons to each room	1.8
Average number of rooms to each family of 5.2 members	2.8

TABLE I.—SOCIAL STATISTICS CONCERNING 36,062 CASES OF PULMONARY TUBERCULOSIS SHOWING NUMBER OF PERSONS COMPARED WITH NUMBER OF ROOMS OCCUPIED.

Rooms in each dwelling.	Number of persons in family.									Total families.
	1	2	3	4	5	6	7	8	9 and over.	
1 . . .	1109	989	777	508	330	168	77	34	33	4,025
2 . . .	48	910	1746	2127	1859	1486	923	558	483	10,134
3 . . .	20	415	1423	2113	2485	2295	1673	1112	1172	12,708
4 . . .	9	131	447	732	922	1028	748	691	1010	5,718
5 and over	6	46	186	287	460	510	561	454	967	3,477
Total .	1192	2491	4573	5767	6056	5487	3982	2849	3665	36,062

Total number of rooms occupied by families of 36,062 patients, the number of whose rooms is given	102,674
Membership of families of 36,062 patients, 5.2 members to family	190,767
Average number of persons to each room	1.8
Average number of rooms to each family of 5.2 members	2.8

The incoming human wave which breaks upon our shores sends its scattered spray to many cities. Too little reaches the country. Too much stays in the city slums. It is entirely natural that this should be the case and that the entering foreigner should seek a dwelling in some locality where his own tongue sounds kindly to his ears. So the Italian, at whatever port he lands, hastens to Little Italy, the Russian seeks Little Russia and the Hungarian finds lodging in Little Hungary.

The State of Pennsylvania varies greatly in its physical and industrial features in its different sections. Consequently, in the communities which comprise the Commonwealth there is noted marked differences in speech and customs of the people. They differ in nationality, creed and intelligence according to the direction and rate of flow of the stream of immigration while the condition of their bodies varies with their individual heredity, environment and mode of life. These peculiarities, however, are the subject of serious study when public health problems demand solution and the broad principles involved are to be applied with the greatest possible benefit to all.



FIG. 1.—Overcrowded bedroom, three beds, six people.

There is no subject which serves as a better illustration of this than tuberculosis, which is constantly being more widely recognized as a community disease. Just as the prevalence of typhoid infection in a community indicates the quality of its sanitary engineering, so the tuberculosis morbidity rate may be used as a criterion of the adequacy of its housing facilities, the character of its industrial conditions and the degree of its social consciousness.

It is common observation that the tendency of recent years, with the great development of industry, has been the concentration of population into cities and towns. With no one responsible for solving their housing problems, what has happened? The overcrowding of land with all sorts and conditions of buildings and

the overcrowding of old houses not adapted for new conditions by the unskilled laborer and his family. The lack of proper planning has resulted in a heterogenous mass of homes, frequently unsanitary, becoming the breeding-place of diseases that affect the whole community.

In studying the character of dwelling occupied by the patients admitted to our dispensaries it is striking to find that the majority of cases come from the so-called private house. This may be readily understood when we realize the construction and location of the average private house in the poorer sections of our cities and the shacks which we so frequently see in the adjacent and rural



FIG. 2.—Dark overcrowded bedroom, four adults and one child. Only ventilation is through a window opening into an inner room.

district—long rows of small dark houses, opening upon courts, thus being deprived of the sunlight, fresh air and being kept in poor repair, subject to damp or wet cellars, poor sanitation and an incubator for an infection such as tuberculosis.

In a report made on 27,277 cases relative to the dwelling place, 23,120, or 84— per cent., cases lived in private houses. These houses differ, of course, greatly as to the number and size of rooms. When one considers that there were 8737 families, composed of from 5 to 9 and over members that lived in 3 rooms, it may be easily seen how unsatisfactory it is to arrange for the management of a tuberculous member.

The most scientific information on ventilation is that air, to be

healthy, must be kept in motion and the humidity kept low. These two factors are more important than the proper proportion of oxygen and carbon dioxide. However, it is advocated that the human organism requires from 800 to 1000 cubic feet of fresh air per hour to keep it in efficient working order. A room $12\frac{1}{2} \times 10 \times 9\frac{1}{2}$ feet is a good-sized room for a slum quarter, yet the number of cubic feet of air which it contains is less than twice the amount required for the health by the average person even if there is not a stick of furniture on the floor. Add the ordinary amount of furniture, every piece of which subtracts cubic feet from the total space, and put four or five or more people in the room instead of two. How much chance does each have of getting the minimum amount of fresh air even provided the air can be completely changed every hour?

Continuing our study, 2412 of these private-house cases were males and classified as being in the incipient stage of the disease, while in this class 2470 were females. There were 997 incipient cases in which the sex was not differentiated.

4908 male cases were classified as moderately advanced and 3213 females placed under the same classification. In 1637 cases the sex was not differentiated.

Of those far advanced, 4210 were males and 2256 females and 1017 cases with sex not given.

Next to the so-called private house, apartments gave the next largest number—namely, 2345 cases, or 8+ per cent. Of these 197 males and 168 females were of the incipient class; 108 cases with sex not stated.

In the moderately advanced class 510 were males and 283 females, while in 212 the sex was not mentioned.

554 males and 201 females were classified as far advanced and 112 sex not given.

Next to the apartment cases comes the tenement group. The cities in Pennsylvania differ from those of some of the other States in that the tenement districts do not play a prominent part in the housing situation.

1019 cases, or 3+ per cent., were found to live in the regular type of tenement house. Of these 103 males were classified as incipient and 75 females; in 43 cases the sex was not stated.

Of the moderately advanced type 244 were males and 116 females; in 63 cases the sex was not given.

It was found that of the far-advanced cases the males exceeded the females almost 3 to 1, there being 235 of the former and 89 of the latter; in 51 cases the sex was not given.

The boarding house is another source of evil, adding 501 cases to the list. Of these 65 were in the incipient stage, 49 cases being males and 16 females; in 27 cases the sex was not mentioned.

Over twice as many cases were classified as moderately advanced, there being 106 males and 32 females and 51 cases with the sex not given.

The far-advanced number is greatest, as 161 males appear in this class and 21 females and 38 cases with the sex omitted.

292 cases were referred from institutions such as hospitals, charitable homes or tuberculosis sanatoria aside from the Pennsylvania State Sanatoria. Of these there were 33 males and 40 females in the incipient group, while in the moderately advanced class 89 were males and 51 females; in 7 cases the sex was not stated.

The moderately advanced class showed the greatest number as 54 males and 13 females, which were classified as far advanced and 5 cases with no data as to sex.

With the exception of the incipient cases under the private-house group, in which the females exceeded the males by 58 cases and the incipient cases under institutions where the females exceeded the males by 7 cases, the largest number of cases appear among the male sex. Considering all the males and females, irrespective of classification, they bear a ratio of 13,865 to 9044 respectively, or a majority of 4821 in favor of the males.

The reasons for the preponderance of the males may be explained in several ways:

1. The males are, in the majority of instances, the wage-earners of the family. Starting with a lowered resistance caused by undesirable conditions at home, poor or improperly cooked or prepared food, poor ventilation, debilitated physical conditions, they are further subjected to the influences of their occupations. The records of last year show that the engineers and surveyors are considerably in the lead of all other members of the professional group, book-keepers and clerks maintain their usual lead in the clerical and official group, commercial travellers in the mercantile group, saloon-keepers and bar-tenders in the public service group and barbers and hair-dressers in the personal service group. The *foreign laborers* outnumber the native in the laboring and servant group. In the manufacturing and mechanical industry group the iron and steel workers come first, with the machinists, tailors, mill and factory operatives, shoemakers, painters and glaziers, carpenters, stationary engineers and firemen, compositors and printers and cigarmakers and tobacco-workers following in the order named. Miners and quarrymen head the list in the agricultural and transportation group, with draymen and hackmen next and steam railroad employes third. The manufacturing and mechanical industry group and the laboring and servant group had the largest numbers respectively.

2. In regard to female occupations the housewife predominates, followed at a great distance by servants, mill and factory operatives, book-keepers, dressmakers and cigarmakers and tobacco-workers.

3. It is also true that men will more readily come to a dispensary for treatment than women, and, furthermore, the latter in many cases are kept busy in their homes looking after the many family duties.

TABLE II.—CHARACTER OF DWELLINGS OCCUPIED BY 27,277 CASES OF PULMONARY TUBERCULOSIS.

Classification.	Sex.	Total.	Private house.	Apartment.	Tenement.	Boarding house.	Institution.
		22,909	19,469	1913	862	385	280
	Male and female ²	4,368 ²	3,651	432	157	116	12
Incipient . . .	Male	2,794	2,412	197	103	49	33
	Female	2,769	2,470	168	75	16	40
Moderately advanced .	Male and female	1,175	997	108	43	27	0
	Male	5,857	4,908	510	244	106	89
Far advanced	Female	3,695	3,213	283	116	32	51
	Male and female	1,970	1,637	212	63	51	7
Far advanced	Male	5,214	4,210	554	235	161	54
	Female	2,580	2,256	201	89	21	13
	Male and female	1,223	1,017	112	51	38	5

² These figures include those cases in which sex was not differentiated.

The nurses associated with the Pennsylvania State Tuberculosis Dispensaries upon visiting a patient's home pay particular attention to the housing conditions, and if bad report the same on the following form to the Division of Housing of the State Department of Health, Mr. John Molitor, Chief:

COMMONWEALTH OF PENNSYLVANIA.

DEPARTMENT OF HEALTH.

Dispensary Housing Report.

DATE..... 191...

Dispensary.....

Name of tuberculosis patient.....

Address.....

Number in family.....

Number of patients in family.....

Number of rooms in house.....

Number of families in house.....

Total number of persons.....

Number of sleeping rooms below ground level.....

Number of windows in patient's room.....

Number of rooms without windows.....

Nurse.

(Reverse side.)

Property owner.....

Address.....

Remarks.....

.....

.....

From that division notices go out for the eradication of the evils and personal inspections are later made by the chief of the division or his assistants in case there is no coöperation or response on the part of the landlord.

It is to be noted how simply the above report card is constructed. Many similar cards used by various organizations are so complicated and require so much time to do the work satisfactorily that little else can be accomplished.

To ensure proper housing of our citizens the above division urges the adoption of the following regulations:

1. Lots must not be built up to the full area with buildings to be used for human habitation.

2. Eliminate all dark rooms which may be used for sleeping and living purposes.

3. No cellar rooms should be used for sleeping purposes, and those used as kitchen and dining rooms should be lighted and ventilated by windows opening directly into the outside air.

4. Stop overcrowding of sleeping rooms and forbid the use of the same beds and bedding by alternating shifts of men.

5. Bath rooms and water-closet enclosures to be lighted and ventilated, and should be easily accessible from the public halls and not located so that it is necessary to go through a bedroom in order to reach same. Each family should have their separate toilet accommodations.

6. Compel connection of all plumbing systems to the sanitary sewer system of the city where possible and prohibit the construction of privy vaults or cesspools on streets which are sewered and also compel the abandonment of all privy vaults and cesspools on properties located on sewered streets.

7. When houses are located on streets that are not sewered, privies must be constructed in a substantial and sanitary manner and maintained at all times in a sanitary condition.

8. There must be adequate water supply for each house, and in each building used for multiple habitation there must be a separate water supply for each family.

9. All houses should be kept in good repair, the cellars free from water or dampness and the premises maintained in a clean and sanitary condition, free from rubbish and garbage.

10. Surface drainage of all kinds, except rain water, should be eliminated and kitchen and laundry wash water should be discharged into the sewer system.

11. Vacant lots, yards of all kinds and private alleys should be frequently inspected and the owners and caretakers or the abutting property holders, as the case may be, should be compelled to maintain them in a sanitary condition at all times.

The following extracts from a recent article by Mr. John Molitor are valuable:

"Will the housing problem ever be successfully solved until more consideration is given to the creation and permanent safeguarding of neighborhoods of considerable area for the man who earns a low wage.

"The more industrious laborer, who with the help of his wife and family, through years of saving, may become able to build himself an attractive, modest, 4-room cottage may soon find his little home between unpainted 1-room shacks and the most undesirable neighbors, or he may find the adjoining lot being used as a junk pen or a huckster's unsanitary yard."

If the houses of the poor are improved the morals, to an important extent, will be improved, and in so doing the health and the relative efficiency will be benefited. As long as slum houses and unsanitary tenements are allowed to exist there will always be people to occupy them.

We must profit by the examples of other nations and be inspired to make possible the pursuit of happiness for our huge army of struggling toilers. We must recognize the need as an economic rather than philanthropic; we must appreciate the ineffectiveness of our elaborate school systems in making good citizens when the influence of the home is opposed to it; we must recognize the evils incident to bad housing.

We must also keep sound and strong the large foreign element which is being constantly woven into our social fabric. Their foreign ideals must be raised to American standards of citizenship, and that cannot be done under the present housing conditions of the poor and dependent, which obtains now in most districts to which they are generally drawn.

CONCLUSIONS. So long as there is no specific cure for tuberculosis we have no means of combating the disease except by adjusting environment, increasing the power of resistance and producing conditions favorable to the prevention and cure of the disease. There can be no doubt that fresh air, proper feeding, cleanliness of person and surroundings, rest, tranquillity of mind, careful regulation of the habits of the patient, and regulated exercise are the factors on which a cure is based. They may therefore be considered as remedies. So long as there is poverty, with all its accompaniments, bad housing, insufficient nourishment, unsanitary conditions of industry, ignorance and many other evils undermining the welfare of society there will be tuberculosis, with its terrible tale of suffering, deterioration and premature death. The hope for better days lies not only in the prevention of the disease but in the eradication of the causes and the existing conditions that influence the spread of tuberculosis.

As the evils of housing are so largely corrected by educational

methods we cannot hope to correct them without the assistance of all educational factors. We are beginning to do what should have been undertaken a long time ago to impress upon the youth while in school the essential lessons of right living.

Children very early in life are susceptible to public health education, and if the elementary foundations of sanitary consciences are well laid in the schools, these pupils when fully grown will be the sanitary educators of the next generation.

FOCAL INFECTIONS IN CHILDHOOD.¹

BY SANFORD BLUM, M.D.,

SAN FRANCISCO, CALIFORNIA.

IN 1869 Winge² reported a case of malignant endocarditis in a man who had died of septicemia originating from an abscess in the foot. Hjelmars Heiberg³ published, in 1872, a case of ulcerative endocarditis occurring in a woman who had died of puerperal septicemia. In both cases, which were studied also by Virchow, chains of elements determined by their microscopic appearance and by their behavior toward chemicals to be of foreign nature were recognized. Here were two cases of focal infection described as such respectively in 1869 and 1872.

The theory of focal infections is by no means new. It has merely been revived and elaborated. Unfortunately attention has recently been concentrated upon certain potential foci of infection to the practical exclusion of others at least equally important. The results are that the subject is being treated in a narrow manner instead of receiving the broad consideration it merits and that diagnosis and treatment are empirically directed within restricted limits instead of considering the potentialities of the entire body. It follows that in cases in which disease is due to an infective focus, avoidable mistakes in locating the focus are frequently made and results of treatment are correspondingly disappointing. Another element in the failure to achieve predicted results is the inclination, consistently followed by physicians, to attribute too many ailments to the reigning idea, in this case to focal infections. It should be kept constantly in mind that not all illness is caused by infective foci.

The term "focal infection" implies three definite propositions:

1. That there exists or has existed a circumscribed lesion or focus.
2. That the lesion is of bacterial nature and as such is capable of dissemination.

¹ Read before the San Francisco County Medical Society, June, 1918.

² *Copstatts Jahresbericht*, 1870, ii, 95.

³ *Virchows Arch.*, lvi, 407.

3. That from the focus there has resulted systemic infection or infection of other contiguous or non-contiguous parts.

The mere presence of pathogenic microorganisms within a circumscribed area does not, *per se*, constitute an infective focus. At most this condition may be regarded as a potential focus of infection. Bacteria—for example diphtheria bacilli—may be harbored indefinitely in a given locality and be perfectly innocuous. They may be non-virulent or walled off or the patient may be immune to their specific action or conditions necessary for their metastatic propagation may be lacking. Failure to recognize this fact has resulted in much misdirected treatment, especially enucleation of the tonsils⁴ and extraction of teeth. For the creation of infections from existing foci two additional factors are indispensable—the bacteria must invade the circulation (hemic or lymphatic) and the part to be infected must be ready for their reception and propagation.

In a paper entitled "The Etiology of Endocarditis, with Special Reference to Bacterial Agencies,"⁵ presented by me in 1902, I stated that, "In general, bacteria pathogenic to the individual could cause endocarditis under the proper conditions: there must be a *locus minoris resistentia* and the bacteria must be present in the circulation." This statement was based upon clinical observations and animal experiments. The experiments consisted in lacerating the endocardia of rabbits by means of a probe introduced through the left carotid artery and subsequent injection into a vein of cultures of pathogenic bacteria. Verrucose endocarditis ensued and in the verrucosities on the endocardia colonies of the injected bacteria—staphylococcus, streptococcus, pneumococcus, *Bacillus typhosus*, tubercle bacillus—were identified. These experiments I published in 1898.⁶ They were artificial focal infections. In the same year I added to the series a case of experimental pyocyanus endocarditis which I published⁷ in connection with the report of a case of pyocyanus endocarditis in a two-and-a-half-months-old infant. This infant had pyocyanus enteritis and became septic; acquired, while under observation, pyocyanus endocarditis and died. In verrucosities on the heart valves pyocyanus bacilli were found. Apart from the fact that this case is unique as the youngest case of bacillary endocarditis reported, it presented all the essential features of a focal infection: (1) pyocyanus bacilli were localized in the intestines; (2) they were found in blood taken autemortem; (3) they produced a specific lesion—pyocyanus endocarditis—in a non-contiguous organ.

It is interesting to note that while much research has in the interim

⁴ Blum: Proper Position of Tonsillectomy, etc., Arch. Pediat., November, 1915.

⁵ Blum: Am. Med., January 17, 1903, No. 3, v.

⁶ Michaelis and Blum: Deutsch. med. Wchnschr., September, 1898, No. 35.

⁷ Blum: Centralbl. f. Bakteriöl., Parasitenkunde und Infek., 1898, No. 25.

been directed toward endocarditis in relation to focal infections, no single fact additional to those enumerated above has been proved. The presence of pathogenic bacteria in the mouth and fauces, with subsequent development of endocarditis, is by no means conclusive evidence that the endocarditis originated from these foci and the complete absence of reports of identification in endocardial lesions of the specific bacilli present in the suspected foci constitutes a deplorable breach in the chain of reasoning. That under proper auspices endocarditis can originate from these sources may without question be assumed; but the frequency in childhood of alveolar disease and tonsillitis when contrasted with the rarity of endocarditis justifies the conclusion that such a sequence is certainly exceedingly rare. (Holt says that in autopsies of more than 1000 children less than three years of age not a single case of endocarditis was found.⁸ Among 1,345,398 school children examined in New York in 1909-1913 less than 1 per cent. showed cardiac disease.⁹) The assumption that streptococci harbored in the tonsils possess especial selective powers against the endocardium and the joints seem unjustified.

Billings¹⁰ reported that Rosenow injected cultures of streptococci obtained from the tonsils into the circulation of animals; arthritis ensued and the deduction was made that the injected streptococci possessed a characteristic which caused arthritis. The fact seems to be that when bacteria are injected into the circulation arthritis occurs as an incident of the induced septicemia. Arthritis commonly occurs with septicemia. Pyogenic bacteria in general manifest a predilection for the serous and synovial membranes. When, as a result of circulatory invasion by bacteria, morbid processes ensue it is usually the serous and synovial membranes that are affected. Meningitis, pleuritis, endocarditis, synovitis occurring in the course of such infections are manifestations of this principle.

Rheumatism is a name used to designate a symptom-complex, the chief characteristics of which are polyarthritis accompanied by fever and pain, with a tendency to implication of the serous membranes, especially the endocardium. As the science of bacteriology has developed and knowledge in this field has increased gradually there have been delimited from the earlier group of cases clinically classed as rheumatism special forms which now are designated arthritis of definite types of bacterial infection—for example, gonorrhoeal arthritis, typhoid arthritis, etc. As knowledge further increases with the passing of time it is to be expected that the group will be still further depleted as other forms of arthritis are recognized, and ultimately rheumatism as a diagnosis will be discarded or accepted as indicating those forms of arthritis of which the

⁸ Holt: *Infancy and Childhood*, 1897, p. 574.

⁹ New York Health Department, Department of Hygiene.

¹⁰ *Arch. Int. Med.*, 1912. *Jour. Am. Med. Assn.*, September 13, 1913.

etiological microorganism is unknown. At different times since the theory of the bacterial etiology of rheumatism has been accepted various microorganisms have been alleged to be the cause of rheumatism. At present the streptococcus is blamed, but there are numerous types and strains of streptococci and evidence of their exclusive guilt is lacking. That the power of attacking serous and synovial membranes is not limited to the streptococcus is obvious on contemplation of such phenomena caused by various other microorganisms, for example so-called typhoid and gonorrhoeal rheumatism, tuberculous meningitis, arthritis and endocarditis, staphylococcus pleuritis, peritonitis, etc. It seems that the selective morbidity is due not to a single specific microorganism but to lower power of resistance to bacterial aggression possessed by serous and synovial membranes. This explains why in infectious processes lesions of the muscles, bones, nervous and connective tissues, though they do occur, are less frequent than lesions of the serous membranes and joints. In childhood secondary foci in the more resistant tissues are commoner than in adults, owing to the comparatively weaker power of resistance of these tissues in childhood. The occurrence of tuberculous hip-joint disease so frequently after a fall or injury may be explained by this theory. Tubercle bacilli having gained access to the circulation from a focus in the lung or elsewhere and lying in wait for a favorable opportunity, secure a foothold in the hip-joint which, as a result of traumatism, offers a *locus minoris resistentiae*. (The terminal artery theory also may be accurate.) Similarly may be explained the selection of the knee-joint and ankle in the teamster as most vulnerable to gonorrhoeal attack, while in the blacksmith the shoulder or elbow is affected by preference. The tonsil appears to have exceptional powers of resistance to focal infectious processes; secondary focal infections of the tonsil are exceedingly rare, though Seawell¹¹ has called attention to their becoming infected secondarily to pulmonary tuberculosis.

Chorea has received much attention in recent discussions of focal infections. On the ground of its frequent association with endocarditis and arthritis its relation to focal infections appears justified, but owing to our ignorance of the pathology of chorea it has as yet not been possible to determine its etiology. Probably chorea is the expression of cerebral cortical irritation due to bacteremia or toxemia. It has not, however, been ascertained what if any role in the etiology of chorea may be played by chemical intoxication and by nervous factors—such as shock. Experimental production of chorea should help to elucidate its etiology. As a working basis for the treatment of chorea, in light of our present knowledge, it seems proper to regard it as the result of bacterial activity. This leads to another aspect of focal infections—namely, to a consider-

¹¹ Jour. Am. Med. Assn., September 9, 1911.

ation of remote or systemic effects of toxemia. This aspect of focal infections differs essentially from the conception presented above. Toxemia is always a potential element and may be an important concomitant of bacterial activity.

An infection is a morbid state due to the invasion and propagation within the body of pathogenic microorganisms. Toxemia denotes a morbid condition produced by the absorption of bacterial toxins.

It is not necessary for the production of systemic or remote effects for bacteria to be disseminated from a localized infection: their toxins may be absorbed and the resultant toxemia may exercise a deleterious influence either upon the general system or upon special tissues or organs. In this way the blood, the nervous system, the heart, kidneys and other tissues and organs may be affected. The injuries inflicted upon the nervous system and the heart in diphtheria are striking examples of this deleterious toxemia. It is probable that toxins are responsible for lowering the powers of resistance of the synovial membranes and thus facilitating the invasion of these structures by bacteria in the production of the various forms of arthritis.

The diagnosis of focal infections consists of two steps: (a) The determination that a morbid state is due to an infective focus. (b) The discovery of the infective focus.

(a) Septic conditions may without hesitancy be ascribed to infective foci. Sepsis by its very nature denotes an invasion by bacteria, and if such an invasion has occurred it immediately follows that the bacteria must have come from some source—*ergo*, a focus. Deep-seated lesions of bacterial nature likewise imply focal origin. Ulcerative endocarditis, septic arthritis, hepatic abscess, septic sinus thrombosis and similar lesions caused by bacteria must have received their original microorganisms from extraneous sources, hence the necessity of a starting-point or focus.

Toxemia may be due to focal infections. Chronic otitis media, pyelitis and tuberculous processes may cause toxemia of focal origin. But other processes also may cause toxemia; for example, in childhood, the always to be thought of eruptive fevers, and these cannot be classed as focal infections. Perhaps a line might be drawn between acute toxic conditions such as accompany the exanthemata, and low-grade chronic toxemias such as characterize tuberculous processes; but the line would have to be elastic and would be somewhat artificial.

The custom of indiscriminately ascribing to focal infections individual symptoms is precarious and unjustifiable. Disturbed sleep, slight temperature variations, headaches, malnutrition, indigestion and anemia may indeed be caused by focal infections; but if so they are indirect results and the direct cause should be sought rather than the uncertain diagnosis "effects of focal infection" hazarded.

(b) When a morbid condition ascribed to an infective source is present the focus of infection should be located. Such a focus may be situated anywhere in the body. An enumeration of the possible sites of infective foci would include the name of practically every tissue and organ of the body. Particularly important sites for infective foci in childhood are the gastro-intestinal tract and the middle ear. The integument, the oral cavity, the nasopharynx, fauces, sinuses, the respiratory tract, the urogenital structures—all may harbor pathogenic bacteria and may furnish infective foci. The presence of pathogenic microorganisms in a certain locality does not constitute it an infective focus. Colon bacilli in the intestines may remain indefinitely and cause no infective process; pyogenic bacteria may be present in the middle ear for years without producing secondary disease; streptococci, staphylococci and diphtheria bacilli may be indefinitely harbored in the tonsils without deleterious effect. Sequential disease must be traced to the primary focus definitely before the diagnosis is assured. This requires the recognition of a primary focus which existed prior to the secondary affection, and it requires that the correlation of the primary and secondary morbid processes be proved. If, during the course of an acute or chronic otitis, mastoiditis or sinus thrombosis develops the sequence is apparent. Recovery of the same type of bacillus from the primary and secondary lesion will prove the connection. But it is possible for a primary focus to be healed when the secondary lesion is discovered—under these circumstances the association is incapable of positive proof—it can only be conjectured. A secondary lesion may become an infective focus. The assertions that “It has long been known that acute rheumatic joint infections are the result of a primary infection of the faucial tonsils or tissues about them—and that acute endocarditis also has its source in many instances from the faucial tonsils” are not borne out by the facts. The synchronous existence of two lesions due to one type of microorganism does not prove that one resulted from the other. Both may have originated from a third, primary, focus or they may have originated from entirely unrelated sources. If what is stated above concerning rheumatism is accepted it becomes apparent that efforts to trace it to a known source must fail. If the disease itself cannot be identified, efforts to trace it to a known origin must prove futile. That endocarditis and arthritis often are bacterial processes and as such emanate from infective foci is clearly established; but that these processes under ordinary circumstances are caused by streptococci which have their primary focus in the tonsils is probably far from the truth—true only to the extent that the tonsils, like other parts of the body, are potential foci which under proper conditions may become active.

As illustrating the liability to err in determining the origin of focal infections the following case reported at the February, 1917, meeting

of the California Pediatric Society may be cited: In a child, infection of the knee-joint was reported as emanating from a tuberculous lung infection. The knee infection occurred four years after the pulmonary affection was diagnosed: the pulmonic process had been quiescent throughout that interval. In May, 1916, tonsillectomy was performed at a local hospital and in July, 1916, six weeks after the tonsil operation, osteomyelitis and endocarditis were present. Tubercle bacilli had never been found in this case and at the time of the osteomyelitis blood cultures yielded, not tubercle bacilli, but *Staphylococcus aureus*. When viewed in an unprejudiced manner it is obvious that the knee infection was not proved as emanating from the lung focus. Almost positively this was a postoperative focal infection, emanating from an infective focus created by the tonsillectomy. Postoperative focal infections are not rare. Septic pneumonias and septic visceral infarcts following operations are focal infections.

Focal infections—endocarditis—following tonsillectomy have been reported by Koplik,¹² Young,¹³ myself¹⁴ and many others. Layton¹⁵ states that arthritic attacks are determined by tonsillectomy. Moore¹⁶ explains how operations cause focal infections.

Treatment of focal infections should be directed along two lines:

1. Treatment of the lesion or condition caused by the infection.
2. Treatment of the infective focus.

Treatment of lesions or conditions caused by focal infections is as multiform as are the results of infection. Sepsis, toxemia, abscesses, endocarditis, nephritis and arthritis should receive the treatment appropriate for those diseases—hygienic, medicinal, serological surgical, prophylactic. Often, perhaps most often, such treatment is the only line applicable owing to inability to locate the source of infection or inability to eradicate it if located. Thus foci of infection in the lungs in pulmonary tuberculosis may cause arthritis, lymphadenitis, endocarditis, toxemia, etc. It is obvious that the inability to eradicate such infective foci renders it imperative that treatment be directed to the secondary lesion or condition. Nor should the value of such treatment be underestimated. Apart from its effects on the secondary lesion the effect of general treatment on the primary focus may be completely or partially successful. Often foci of infection heal spontaneously and improvement in nutritional status, in hygienic conditions, increases power of resistance to bacterial processes. This is the most successful principle of treatment as yet employed in combating pulmonary tuberculosis—always a potential focus of infection—and has yielded most gratifying results, many cases as result of such treatment being reported

¹² AM. JOUR. MED. SC., July, 1912.

¹³ Boston Med. and Surg. Jour., 1915, p. 173.

¹⁴ Blum: Laryngoscope, September, 1915.

¹⁵ Lancet, 1914, i, 1106.

¹⁶ Med. Record, December 2, 1916.

cured. If not indeed cured they are at least practically cured and to all appearances and effects the patient is restored to complete health.

There are cases which, on account of their greater importance and danger to life, compel treatment of the secondary lesion irrespective of its etiology or treatment of possible primary foci. Such cases as sinus thrombosis and brain abscess, even if their focal origin from chronic otitis is plainly established, demand immediate treatment while the primary focus can wait.

Eradication of the primary focus of infection is certainly to be desired, but, as has been stated, it is not always feasible. In toxemia due to a localized abscess, putrefaction in the intestines, etc., cure of the focus may alone be sufficient treatment. But to assume that in cases in which a distinct metastatic bacterial process has been established, as in endocarditis or arthritis, eradication of the primary focus will cure the secondary lesion is fallacious. Such processes, once established, are self-supporting: the most that can be expected from removal of the primary focus under such conditions is that the possibility of further deleterious increments from the original source would be excluded. The question whether treatment should be aimed at cure of the infection or removal of the infected structure must be decided on its merits in each individual case. The creation, by operative interference, of foci of infection constitutes one of the most important facts in consideration of this subject. Evacuation of abscess cavities, removal of diseased appendices, surgical relief for otitis media and mastoiditis require no comment for their approval. Far differently must be viewed the promiscuous practice of tonsillectomy. Shambaugh's¹⁷ statement that "No one believes the tonsils should be removed without an indication" is erroneous. Perry presented at the 1911 session of the Pacific Coast Otoöphthalmological Society a paper advocating tonsillectomy in all children four years of age as a prophylactic measure. Others who participated in the discussion endorsed his views. Too often this procedure converts an innocuous nidus into a virulently infective focus. In straightening of the teeth, care should be taken to avoid such mistakes. Complicated mechanical apparatus employed in orthodontia affords excellent opportunities for bacteria to congregate and the forcing of teeth about in their alveolar sockets opens to the assembled bacteria inviting avenues for invasion. Nervous and digestive disorders result. I have seen cervical adenitis traced to tooth manipulation. The teeth and the tonsils have long and blamelessly occupied their respective positions. Now they are being violently assailed. No blanket indictment should be received against them. But unless in each individual case they are proved guilty of flagrant crimes they should not be ruthlessly uprooted.

¹⁷ Eye, Ear, Nose and Throat, 1916, vol. iii.

The surgical procedures of tonsillectomy and tooth extraction are being employed as a diagnostic measure. Physicians assert that in some cases of disease of obscure origin removal of the tonsils is followed by prompt alleviation of symptoms and that the difficulty lies in determining which cases will react favorably to the operation. They frankly state that they do not know whether the tonsils are at fault or not, but they attempt to justify the operative procedure on the plea that if it proves not beneficial the operation is innocuous.

This common practice of tonsillectomy as a diagnostic measure is reprehensible and should be discontinued because it is unscientific in that it is a surgical procedure undertaken without definite indication, it is attended with danger (*cf.*—creation of infective foci and fatalities due to pulmonary embolism, hemorrhage), and it diverts attention from other diagnostic procedures which not infrequently would disclose obvious causes of the disease.

CONCLUSIONS. 1. Focal infections imply:

- (a) Presence of primary focus of pathogenic bacteria.
- (b) Invasion of circulation by bacteria or toxins.
- (c) Sequential effects.

2. Focal infections comprise an important class of morbid conditions in children.

3. Various bacteria may operate in focal infections, in general all pathogenic bacteria.

4. The pyogenic bacteria are the common agents in focal infections.

5. All the tissues of the body may be involved in focal infections: the serous and synovial membranes are specially susceptible to secondary involvement.

6. The frequency of involvement of the joints and endocardium in focal infective processes is not due to selective action of the microorganisms but is due to greater susceptibility of these structures to bacterial invasion.

7. Rheumatism is a name used to designate some types of arthritis of the bacterial etiology of which we are ignorant. Its use will probably become more restricted and eventually be discarded as various types of arthritic infection are discovered.

8. Effects of focal infections are twofold, septic and toxemic.

9. Diagnosis requires recognition of a morbid process as secondary and tracing of it to its source.

10. Treatment should be:

- (a) Systemic and local.
- (b) Directed to the secondary state and to primary lesion.

11. Treatment may be directed either to cure of the infected area or eradication of the focus.

12. Focal infections may be created by operative procedures such as tonsillectomy and orthodontia.

THE COMPARATIVE VALUE OF RADIUM AND ROENTGEN RADIATION.

By RUSSELL H. BOGGS, M.D.,

ROENTGENOLOGIST, ALLEGHENY GENERAL HOSPITAL; DERMATOLOGIST AND
ROENTGENOLOGIST, COLUMBIA, PITTSBURGH AND ST. FRANCIS'S
HOSPITALS, PITTSBURGH, PA.

MANY contend that the radiation from the roentgen tube and radium are the same, but this we know is only partly true. There is a difference in the physical properties between the two forms of radiation as well as a somewhat different physiological action on both diseased and healthy tissue. In a great many instances those using only the roentgen rays will say that all can be accomplished with this form of radiation that can be accomplished by both radium and the roentgen rays, while those who only employ radium may make a similar statement or may even say that radium is superior alone in all cases in which radiotherapy is indicated. Such statements show that the radiotherapeutist is not familiar with both forms of radiation and has not treated a large number of cases by both methods.

Physicists have demonstrated that if electric current of high voltage be passed through a glass vacuum tube it is filled with special fluorescence and produces certain forms of radiation depending upon the degree of vacuum. That certain rays, such as the anode, cathode and roentgen rays, are produced respectively analogous but not identical with the alpha, beta and gamma rays of radium. The anode and cathode rays are not employed at all as they do not pass through the glass walls of a tube and the alpha rays from radium are cut off by thin sheets of paper, so we are only dealing with the beta and gamma rays from radium and low and high penetrating rays from a roentgen tube. The roentgen rays are very similar to gamma rays, and when they are absorbed by living tissue produce a similar reaction. The beta rays from radium are very active, but are limited in their penetrating power, while the highest gamma rays will penetrate lead and metals of great thickness. It is generally conceded that it is the rays which are absorbed in the tissues and the secondary radiation set up therein which produce the change in the tissues. The difference in the physiological action between radium and the roentgen rays may be due to radium giving off beta rays, and that the gamma rays from radio-active substances set up more intense secondary or beta rays than from a roentgen tube.

It is not my purpose to describe the physical properties of radium and the roentgen rays, because my paper pertains to the clinical side of the subject.

Radium and the roentgen rays are closely related in their action

on tissue and should be discussed or considered together. Both forms of radiation have the so-called selective and inflammatory action on living tissues. Each will produce a destructive inflammation if given with sufficient intensity, but with radium a reaction of a much greater degree can be produced without permanently injuring healthy tissues than with the roentgen rays. This is an important therapeutic difference between the two agents and is very important when treating some lesions. Therefore, radium can be used therapeutically with a greater destructive power locally than the roentgen rays, but great care must be exercised, particularly so if cosmetic results are desired. This explains why radium is superior in the treatment of cancer of the uterus and rectum, epithelioma of the lip, mouth, throat, eyelids or lesions situated on the mucous membrane as well as its ease of application in cavities.

In order to produce tissue changes, either by radium or roentgen rays, it is necessary that sufficient quantities reach the tissue to be treated and not destroy adjacent healthy tissue or tissue through which the radiation must pass. When a tube of radium is brought in contact with the growth a certain dosage will inhibit proliferation and finally cause necrosis of the cells nearest it, while farther away from the tube the same kind of cells will only be stimulated. Therefore, there is a limit through which the rays can pass through healthy tissue without producing destruction and destroy cancer cells. It has been demonstrated that when radium is placed in contact with a cancerous mass that the malignant cells can only be destroyed from $2\frac{1}{2}$ to 4 cm., or a little over an inch from the radium tube. By cross-firing this can be increased somewhat, but will not take the place of the source of energy being placed 7 or 8 inches.

Radiation to the depth of from $\frac{1}{2}$ to $1\frac{1}{2}$ inches is usually sufficient to destroy most cancerous growths, but it will not reach the outlying cells in the lymphatic glands. Deeper effects can be obtained by placing the source of energy at a distance from the mass to be treated and by cross-firing. By placing the radium or the roentgen tube 8 inches from the surface and treating through seven ports of entry a tumor 4 inches below the surface will receive about the same amount of radiation the skin of any one area receives. Then since most malignant cells are about two to five times more susceptible to the destructive action of the rays than normal tissue, it has been possible to produce clinical retrogression of malignant growths, and even within the lymphatic glands at some distance from the surface, without destroying the overlying skin. With the roentgen rays there is sufficient energy with the tube placed at 8 inches from the surface, but with radium the supply is limited, and even those having the largest amounts have not enough to place it at this distance and treat large areas in a reasonable length of time.

When the radiation must reach tissue beyond $1\frac{1}{2}$ inches from the surface the widely distributed roentgen rays have the advantage of any amount of radium which has been employed up to the present. The distance of radium, even if the growth is only 1 or 2 cm. below the surface, is important in deciding on the dosage, in order that the radiation is not too intense on the surface and too weak on the opposite side of the growth. In giving radium there are a number of factors in the specifications of a therapeutic dose.

In some cases, by inserting radium into the growth, larger amounts of tissue can be destroyed, but we are well aware today that whenever a cancerous mass is opened and not completely removed it nearly always hastens metastases, the same as an incomplete operation. Therefore, I never advocate inserting radium into a cancerous growth unless the surrounding lymphatics have been thoroughly treated and the cancerous mass at least partially walled off.

From a clinical stand-point, all things being equal, radium and the roentgen rays may be divided into two classes: namely, those in which a localized reaction is desired radium is to be preferred, and those in which large areas are to be treated the roentgen rays are to be preferred. In many instances radium should be used locally while the adjacent lymphatics should be treated by the roentgen rays. The exact comparison of the two forms of radiation is extremely difficult, due to the wide difference in technic and the wide variation of results reported by the various writers. This is further confused by many physicians, employing both forms of radiation, who have not familiarized themselves with either radium or the roentgen rays and who have not made a careful study of the diseases under treatment and of what can be expected from other methods of treatment.

No tissue is unaffected either by the rays from radium or the roentgen tube, provided the intensity be sufficiently great and the exposure sufficiently long. In general the rays in small doses have a stimulating and in large doses a destructive action. There is always a latent period after the application of the rays or occurrence of changes in the tissues. The larger the dose the shorter the latent period will be. Every kind of tissue acts in its own specific way. The gland cells will be destroyed by a dose which does not harm the cells of the connective tissue or the skin; in other words, the sensitiveness of the action of the rays varies with the type of cell, and this is what is meant by the selective action.

The lymphatic organs are very sensitive to the rays' action being cicatrized by the destruction of lymphoid cells; under much larger doses muscle tissue degenerates. Cartilage is very little affected even when large doses are given, and the endothelium of the small bloodvessels is extremely sensitive to radiation, and with comparatively small doses swells up enormously and completely obliterates

the lumen of the vessels, while large doses causes its destruction. There seems to be a marked difference between the action on the small bloodvessels; that is, the endothelium is much more susceptible to radium than to the roentgen rays. This is most likely the reason that superior results in the treatment of vascular nevi are obtained with radium.

Diseased tissues are more easily influenced by the use of either radium or the roentgen rays than normal healthy tissues. The action of the rays varies considerably with the type of disease under treatment. It requires considerable less radiation to destroy sarcoma in the lymphatic glands than it does to destroy carcinoma. This could be illustrated by treating lymphosarcoma of the cervical glands where there is a large mass and in treating carcinomatous glands which have metastasized from the lip, tongue or throat. The large sarcomatous mass will disappear much more quickly under the same amount of treatment than the small carcinomatous glands. The results obtained in the treatment of sarcoma of the mediastinum are very marked when treated with radium or the roentgen rays externally in comparison with mediastinal involvement from carcinoma of the breast. If observed by roentgenograms, sarcomatous masses will respond rapidly while carcinomatous masses will decrease slightly or the growth will only be inhibited. There is a difference in the two diseases responding to the same amount of radiation, which has led to much confusion, and unless the radiotherapeutist is familiar with these facts he is very likely to make mistakes in drawing his conclusions.

As before stated, in treating 4 inches below the surface of the skin it is necessary to give seven doses through different skin areas in order to obtain an erythema dose 4 inches below the skin. Carcinoma will not be much affected unless this amount of radiation is given, while a sarcomatous mass would probably be reduced in size by from one-third to one-fifth of this amount of radiation. We know that many have reported excellent results by applying radium externally near the skin in sarcoma of the mediastinum, while the same results have not been reported in carcinoma, as too small amounts of radiation would reach the mediastinum even with cross-firing, without permanent injury to the skin, unless the energy was placed at a distance in order to give almost a homogeneous ray 3 or 4 inches below the skin.

It is a rule in the treatment of both carcinoma and sarcoma to give as heavy a dose as the normal tissue will stand and treat the glandular tissue as far away from the growth as possible. There is also a difference in the response of tubercular adenitis and carcinoma involving the lymphatic glands. Tubercular adenitis responds much more quickly than carcinoma, but not nearly so quickly as sarcoma of the glands; but the results in tubercular adenitis are usually permanent while in sarcoma they are more

often only temporary. It is also a well-known fact that epitheliomas of the rodent type respond to less radiation than those of the squamous variety, because it requires so much more radiation in order to cure squamous epitheliomas and because the adjacent glands are so early invaded is no reason for many of the statements which have been made: that is, that this type should not be treated by radiation.

It is also true that an epithelioma situated on the mucous membrane is always more malignant in character than that where it starts on the skin. In order to produce results in the mouth and throat it is always necessary to produce a marked reaction, and this should be done promptly.

Experience in the physiological actions of both radium and the roentgen rays must be thoroughly mastered, as well as a careful study of the pathology of the different types of tumors and the manner in which each spread. Many of our best roentgenographers are very poor radiotherapeutists simply because they have not made a careful study of this branch of roentgenology. Fourteen or fifteen years ago, or in the early days of roentgen therapy, many rash statements were made, and if it had not been for those specializing, sifting the good results from the bad, roentgen therapy would have long ago been discarded as useless.

Five or six years ago, when radium was taken up in the treatment of cancer the newspaper notoriety prejudiced many physicians against its use, and if it had not been for a few persistent workers it would soon have been discarded. Radium by many physicians was looked upon as a fake cure. Today things are rapidly changing and both radium and the roentgen rays are being advocated by many of those who formerly condemned their use. The last year or two nearly all text-books of surgery have added a chapter on radium therapy. This is gradually educating the medical profession to the uses of radium and the roentgen rays.

The ones best versed in the treatment of malignancy and who know the limitations of each method are taking up radiotherapy much more readily than those who have only operated upon a few cases. Experience is the best teacher and a large number of failures by any method is the best cure for radicalism. I do not mean to belittle surgery, because much has been accomplished by this method, but surgeons should know their limitations as well as those using radium or the roentgen rays.

The time is far distant when the profession as well as the public are going to make this demand.

In discussing the comparative value of radium and the roentgen rays, malignancy, with its different types and locations, goitre, tubercular adenitis and fibroids will be discussed separately, because there are many factors which play important parts in the treatment of each condition and should be carefully considered in determining

the proper radiation for each particular case. I have already pointed out the difference of susceptibility in the various types of tumors to radiation as well as the manner in which different healthy tissue reacts.

The treatment of malignancy demands specialized study, and every physician or surgeon who treats malignancy should know its various forms and stages, and also know what has been accomplished by radium, roentgen rays or any other method by which results have been obtained. In treating malignant growths with either radium or the roentgen rays it is our object to destroy the cancer cells without permanently injuring healthy tissues. Our problem therefore is to expose a tumor for the sufficient length of time, with the proper amount of radiation to cause its disintegration, while the healthy tissue receives only such an amount that no harmful effects are produced.

Assuming that we have properly diagnosed the case we must decide what form of radiation is best suited, radium or the roentgen rays, or a combination of both. There are many serious drawbacks to any method of dosage; this can only be mastered by experience and judgment. Today radiotherapy is a recognized method of treatment in postoperative cases, recurrent and metastatic, primary inoperable, and primary cases.

CARCINOMA OF THE UTERUS. In the treatment of carcinoma of the uterus up to the present time this method has usually only been employed in the hopelessly inoperable or recurrent cases. In these classes of cases various reports show that in from one-quarter to one-third of the cases, that the carcinoma disappears locally, and the patient is locally or clinically cured, but when there are extensive metastases the treatment is only palliative. In many of these cases metastases had taken place before they were referred for treatment. Often deep metastases cannot be determined by physical signs. Nevertheless, the palliation is more satisfactory, and possibly adds from four to six times to the life of the patient as compared to any other palliative measure; and even hopeless cases have remained well for more than three years. After radium treatment the local effects are very striking; the bleeding diminishes and disappears and the offensive discharge is checked and becomes odorless. The local condition changes in character usually within two to four weeks after the first treatment has been given, and the cancerous mass begins to contract and shrink and continues to diminish in size. This is more marked in some cases than in others, the growth having entirely disappeared within two months. The treatment should then be repeated, but the time and dose must be decided upon by existing conditions.

When the pain and offensive discharge disappear the patient's general health improves rapidly. This even occurs in some patients who are in a toxic condition and have been taking morphin; the

pain is relieved and no medication is necessary, and the patients are restored to perfect health for a time at least.

There is a difference of opinion in regard to the technic of applying radium in uterine carcinoma. Many advise the use of very large quantities of radium, while others advocate the use of smaller quantities applied for longer periods. All have generally agreed that less than 50 mg. of the element should not be employed in uterine carcinoma. Many prefer to use from 50 to 100 mg., using it a sufficient length of time to give from 2000 to 4000 mg. hours within the first week or ten days; the dose must always be decided upon for each individual case. Some give this quantity at one seance while others divide it up into six or eight. The results seem to be about the same, but the condition of the patient should possibly determine the course to pursue.

The writer cannot too strongly advocate that radium be supplemented by the roentgen rays, feeling sure that by using from 50 to 100 mg. applied locally with proper roentgen therapy from without are superior to any quantity of radium used alone.

Kelly and others are using radium at a distance of from 2 to 5 inches from the surface, in large quantities from without, in the same way as many are using roentgen therapy from a Coolidge tube. Whether their results are equal or superior remains to be seen.

CARCINOMA OF THE RECTUM. The results obtained by the use of radium in carcinoma of the rectum vary greatly and cannot be compared to the results obtained in carcinoma of the uterus. If a sufficient amount of radium is given a proctitis generally occurs which is very troublesome unless a colostomy is performed. Most of those using radium in the treatment of carcinoma of the rectum advocate colostomy before beginning or within a week after the first treatment. This prevents the feces from aggravating the radium reaction and avoids tenesmus, which always occurs if a full radium dose is given and where a colostomy has not been performed. Where a colostomy has been performed and larger doses of radium have been employed a few inoperable cases of carcinoma of the rectum have been apparently or temporarily cured. If the patient will not consent to having a colostomy performed the same amount of radiation cannot be given, and palliation is all that can be expected.

Carcinoma of the bladder has not responded nearly so well as carcinoma of the uterus. Unfortunately, the cases are usually not diagnosed until late, and besides it is more difficult to apply radium to the bladder than to almost any other organ of the body. A few good results have been reported, and everyone using radium has obtained marked palliation in a number of cases. This palliation lasts from one to three years.

I had a patient referred to me with carcinoma of the prostate

who was much pained, and could only urinate with difficulty. A month after the first treatment he could urinate freely and had no more pain for over a year. During the next six months his pain returned, but he was in better condition eighteen months after the first treatment than when he was referred to me. From this time on he gradually became worse and he received very little further palliation from the treatment.

Young, in discussing the uses of radium in the treatment of cancer of the prostate and bladder, states that while it is not his intention to speak of the ultimate results it can safely be stated that truly astonishing results have been obtained in some cases: namely, disappearance of obstruction, shrinkage and great softening of certain cancers of the prostate and extensive retrogressive changes in inoperable cancers of the bladder. The methods devised by Young offer a new fertile field of therapeutics in a class of urological cases which heretofore have been almost beyond relief. While we do not as yet know all the possibilities of cure we do know that much relief can be afforded.

EPITHELIOMA. Radium and the roentgen rays in general should be considered as a routine method in the treatment of epithelioma, because when properly applied practically all the epitheliomatous tissue can be made to disappear, and there are fewer recurrences than by any other method. Today it is considered a perfectly legitimate method of treatment in proper hands, but is a method liable to abuse if it is not restricted to its proper field.

It is generally believed that equally good results can be secured in small epitheliomas situated on the skin, by either radium or the roentgen rays; but when an epithelioma is situated on the mucous membrane and involves the lower lip, mouth or throat, or invades cartilage, radium is much superior to the roentgen rays. However, I believe that much quicker results can be obtained in even the small epitheliomas situated on the skin by radium.

Epithelioma of certain locations on account of special features warrants brief separate description. This is on account of the nature of the tissues as well as the lymphatic supply. The virulence of an epithelioma increases or decreases proportionately with its richness or poverty of lymphatic supply. In giving a prognosis of an epithelioma, besides location, the several factors to be considered are in the variety, extent, duration and rapidity of the process. In all instances the earlier the treatment is instituted the less chance is there of a recurrence. In many superficial forms the disease if neglected is slow in its progress, but eventually it will become dangerous to life if left untreated. In the earliest stages, when the disease is limited to the face and is of superficial type, treatment is almost invariably successful and permanently so. Even when moderately advanced the results are usually favorable. The same may be said of the deep-seated and papillomatous

forms if not of too long duration, but in these cases glandular involvement occurs early. Cases of long duration in which marked destruction has already taken place and in which there is considerable infiltration of the surrounding tissues the prognosis as to a permanent cure is not so favorable, and particularly so if the glands are invaded. Rodent ulcer is very amenable to treatment early, but when allowed to have full sway and when it covers a large area it is of a serious nature because this type of epithelioma seldom invades the glands but destroys everything in its way.

The end-results of epithelioma of the lower lip have been discussed by many, and some believe that these cases should be treated with radium locally and the adjacent glands by the roentgen rays rather than a surgical operation. Today the general practitioner frequently refers these cases to the radiotherapist in the first instance rather than to the surgeon.

Any method in the treatment of epithelioma must be one which completely eradicates every cancerous cell. Experience has taught us that an epithelioma in this situation is rather a regional than local lesion. For this reason early surgical removal, wide and radical, has proved inefficient, because a recurrence takes place in over 50 per cent. of the cases when there are no palpable glands at the time of operation and in over 75 per cent. when there is any glandular involvement. All precancerous lesions should be removed by some method without leaving any scar whatever. Many believe the results by radiotherapy (meaning radium and the roentgen rays) are equal and even better than those by surgery, and that the removal should only be done in selected cases. There are a number of radiotherapists who have had sufficient experience in epithelioma of the lower lip whose results justify them in considering radiotherapy a perfectly legitimate method of treatment.

In the treatment of malignancy of the mouth and throat with radium, results have been obtained in a sufficient number of cases to entitle its use to consideration in every case whether alone in small lesions, as an antioperative procedure or as a palliative method in hopelessly inoperable cases. And since even the smallest lesions are very prone to recur locally, and the adjacent glands are so early invaded, radiotherapy should follow surgical removal of even the smallest growth.

Sarcoma in the nasopharynx is much more amenable to radium treatment than carcinoma. Sarcoma, even in cases in which half the throat is filled with the growth, will frequently disappear in from four to six weeks after radium treatment. One such patient whom I treated with radium has remained well two and a half years. This is really remarkable, because his throat was almost filled with a mass and he could scarcely swallow or speak above a whisper. I had another patient in whom the sarcoma started in the tonsil; three operations had been performed, and within five weeks after

the last operation there was a recurrent mass which filled two-thirds of the throat. Within six weeks after radium treatment the growth had entirely disappeared. Did time permit I could report quite a number of similar cases. In most of these cases, however, the time elapsed since the treatment was given has not been sufficient to warrant these being called more than clinical cures.

While, as before stated, carcinoma of the mouth and throat is not so amenable to radium as is sarcoma, still some results have been obtained. For the sake of description I call the lesions which are very superficial, epitheliomas and those which have invaded the deeper tissues carcinoma. If ulceration is confined to the superficial layers of the buccal mucous membrane and has not spread to the teeth one application of radium will frequently heal the lesion. But if the ulceration has to any extent invaded the muscle tissue it is very resistant to radium treatment. Such cases should be given sufficient radiation to produce a marked reaction. This will usually disappear in from two to four weeks; then electric coagulation should be employed rather than a repetition of radium. This will usually heal promptly, leaving very little scarring and no contraction of the surrounding tissues. If the gums are involved the teeth seem to act as an irritant and the cancerous process spreads readily, but if they are extracted it seems to only aggravate the condition.

What has just been said in regard to the buccal mucous membrane will apply to the tongue, except that the muscle tissue is earlier infiltrated, and the glands are earlier invaded.

The treatment of carcinoma of the breast by the roentgen rays has been carried out by many during the past fifteen or sixteen years and is today a recognized method in the treatment of post-operative cases, recurrent and metastatic, primary inoperable and primary cases that cannot be operated upon. For a long time it was taught and accepted as a truth beyond dispute that the only proper and scientific method was the radical operation; that is, the immediate surgical extirpation of the growth even in the hopeless stages. But things are rapidly changing and today it must be recognized that surgery which was taught for so long as the only method is really only part of the treatment. And while operation still holds first place in the early cases, even at this stage it should be supplemented by roentgen therapy. This sentiment is spreading among some of the leading surgeons who, in the past, did the most radical operations for cancer of the breast at any stage, and it springs mainly from comprehensive experience with a great number of cases traced out carefully to their end-results. Roentgen therapy is taking the place of the ultraradical operation, such as removal of the supraclavicular glands or the clavicle.

The treatment of carcinoma of the breast by the roentgen rays has, comparatively speaking, passed through the same stages as

surgery. The early stage might be compared with surgical treatment of a quarter of a century ago when surgeons only amputated on the breast. Our technic in the beginning was very crude; we neither used filters nor had a standard dose, and we omitted important chains of lymphatics in which metastases frequently occurred. Indeed, it is quite remarkable that a creditable number of good results were obtained when one considers the inefficient equipment and faulty technic which were employed.

All roentgenologists agree that each case should have a full physiological dose or all that the skin will stand, not only to the anterior chest wall, but to every chain of lymphatics draining the breast as well as to the opposite side of the body. The location and stage of the tumor as well as the kind of operation performed, and the physical condition of the patient, must be considered carefully in deciding on the treatment. I believe from two or three times the usual dose of radiation can safely be given in the supraclavicular region and in places in which there is no scar, and in which the cutaneous circulation has not been interfered with by the operation. A study of the supply of the lymphatics and the manner in which they metastasize should be made by every one treating carcinoma of the breast. This will never be done by the non-medical technician. In fact, too little attention everywhere has been given to the supply of the lymphatics, their depth and extent and the best manner of thoroughly radiating each chain. Raying the lymphatics sufficiently to the proper depth and as extensively as metastases take place is indeed no easy task. It requires just as much care and judgment as the most careful dissection. Efficient radiation makes operation more radical, increases the percentage of cures in early as well as in more advanced cases and delays recurrence in all cases.

It has been pointed out by competent surgeons that when an operation was performed before a diagnosis could be made clinically without a microscope that 80 per cent. of the cases could be cured. Deaver and McFarland in their recent book, *The Breast: its Anomalies, Its Diseases and Their Treatment*, make the following statement: "It has been stated that 80 per cent. of patients in whom the disease is confined to the breast, as proved by both macroscopic and microscopic examinations of the tissues adjacent to this organ, are permanently cured of their diseases by the radical operation. Therefore, a patient presenting a small movable mass localized to the breast can be assured that 4 out of 5 cases of a similar nature are cured by operation. When axillary lymph nodes are palpably enlarged as the result of metastases the chances of operative cure are at once diminished to one in five." They further say: "In the opinion of many surgeons involvement of the supraclavicular glands is a contra-indication against operation."

The absence of palpable enlargement does not always mean an

absence of carcinomatous involvement. Halstead found that notwithstanding the present-day extensive operation, death from metastases occurs in 23.4 per cent. even in cases with microscopically negative axilla. A few years ago scarcely any of the physicians or surgeons realized the importance of this, and even today there are some who are operating on late or advanced cases and are expecting the same results that the leading authorities obtained in early cases.

Retraction of the nipple, axillary and supraclavicular involvement are late symptoms from a prognostic stand-point. Physicians who talk about favorable cases for operation when the nipple is retracted as well as when the axillary and supraclavicular involvement is present should read Deaver's book, from which I have just quoted; in fact, anyone treating cancer of the breast should read this book carefully and many would not be so radical from the surgical stand-point and would appreciate more the value of the roentgen rays.

Deaver questions whether as much palliation is received from operative as from non-operative methods, and expresses his general dissatisfaction with operations of a palliative nature in the treatment of carcinoma of the breast, since in certain cases the disease has been excited to greater activity by an incomplete operation and the life of the patient considerably shortened. In this connection he mentions the unreserved statement of Bloodgood that "Incomplete operation hastens death."

He further states that since 1897 extraordinary advances have been made in roentgenotherapy that remove most of the indications for the ultraradical operative procedures which have practically no curative value and a primary mortality of at least 25 per cent.

In the past many have given a few treatments over the line of incision, axilla and supraclavicular areas. Such treatment is very incomplete, since it omits those lymphatics which frequently metastasize: namely, suprascapular, anterior pectoral of the opposite side, internal mammary, subscapular, paravertebral, xiphoid and inguinal group. A study of bone metastases makes us realize how extensively the lymphatics become involved. It is known that metastases may occur in distant glands at a very early stage of the disease. While the axillary glands are the most frequently involved (indeed, so frequently involved that the microscopic freedom at the time of operation is the exception) in some cases they are free when there is involvement of the abdominal or other internal viscera. The value of palpable glands is overestimated. The lymphatics in the axilla may become enlarged by previous infections of the arm or breast. Therefore, it requires judgment and in some cases microscopic examinations before the cause of enlargement can be positively determined. Metastasis, too, varies with the different types of tumor and occurs earlier in the

young and fat patients, owing to the greater richness of the lymphatic supply. Efficient roentgen treatment must take care of these variations.

It is generally conceded that the smaller the caliber of the lymphatics, as well as the greater the degree of senile atrophy, the greater the tendency to oppose cancer dissemination. If the roentgen rays did nothing more to adjacent lymphatics than produce a sclerosis the treatment would still be indicated for retarding the disease. The frequent involvement of one breast to the other is due to the distribution of the lymphatics of the chest wall. Autopsy has shown that the liver metastasizes more frequently than any of the internal organs, and in many cases becomes involved in comparatively early stages.

INFLUENCE OF RADIUM WATER THERAPY ON CREATININ AND URIC ACID METABOLISM IN CHRONIC ARTHRITIS.

BY F. H. McCRUDDEN, M.D.,

AND

C. S. SARGENT, S.B.,

ROBERT B. BRIGHAM HOSPITAL, BOSTON.

IT seems to be well established that ingestion of water impregnated with radium emanation is highly effective in the treatment of certain forms of chronic arthritis. An analysis of 471 cases of chronic arthritis under radium therapy reported by thirteen authors showed definite improvement in 391 cases, of which 102 were practically cured.¹ Out of 165 cases of gout all but 16 showed improvement, but despite numerous studies we do not yet understand the *rationale* of the radium therapy.

The special effectiveness of radium therapy in gout directed early attention to the influence of radium on the uric acid metabolism. As a result of the investigations in His's clinic, it was affirmed that uric acid occurs in the blood in gout in a specially insoluble modification and that under the influence of radium this insoluble pathological form of uric acid becomes changed to the more soluble physiological form, which is easily destroyed and excreted, the net result being a rapid solution of the gouty tophi,

¹ Rowntree, L. G., and Baetger, W. A.: Radium in Internal Medicine: its Pathological and Pharmacological Effects, Jour. Am. Med. Assn., 1913, ii, 1438.

an increased elimination of uric acid in the urine and a disappearance of uric acid from the blood.²

The experiments on which these investigators based their theory of gout and the action of radium were at first apparently confirmed.³ But more carefully controlled observations, with reliable methods, have failed to confirm them. Radium does not appear to influence the rate of uric acid decomposition,⁴ the solubility of uric acid,⁵ the uric acid content of the blood⁶ or the rate of uric acid excretion.⁷ Further study of the subject seems therefore desirable.

At the Robert B. Brigham Hospital we have had an opportunity to study the influence of radium on the metabolism of three patients with chronic arthropathies: A man, aged eighteen years, with the

² Gudzent, F.: Physikalisch-Chemisches Verhalten der Harnsäure und ihre Salze im Blut, *Ztschr. f. physiol. Chem.*, 1909, lxxiii, 455. Gudzent, F.: Der Einfluss von Radium auf die harnsäuren Salze, *Deutsch. med. Wehnschr.*, 1909, No. 35, i, 920. Gudzent, F., und Loewenthal: Ueber den Einfluss der Radiumemanation auf den Purinstoffwechsel, *Ztschr. f. klin. Med.*, 1910, lxxi, 304. Gudzent, F.: Einiges über die biologischen Eigenschaften der Radiumemanation und ihre Anwendung bei Krankheiten, *Radium in Biologie und Heilkunde*, 1911, i, 14. Gudzent, F.: Klinische Erfahrungen über die Behandlung der Arthritiden und der Gicht mit Radiumemanation, *Radium in Biologie und Heilkunde*, 1911, i, 132. Gudzent, F.: Klinische Erfahrungen über die Behandlung der Arthritiden und der Gicht mit Radiumemanation, *Berl. klin. Wehnschr.*, 1911, xlviii, 2098. His, W.: Die Behandlung der Gicht und des Rheumatismus mit Radium, *Berl. klin. Wehnschr.*, 1911, xlviii, 197.

³ Uric Acid Destruction by Radium. Mesernitsky, P.: Die Zersetzung von Oxypurinen durch Radiumemanation, *Zentralbl. f. inn. Med.*, 1912, p. 573. Diminution or Disappearance of Blood Uric Acid under Radium. Mesernitsky, P.: Ueber die Schädigung des Organismus durch hohe Dosen von Radiumemanation, *Arch. f. physikal. Med.*, 1911-12, vi, 50. Falta, W., und Zehner, L.: Ein Fall von Gicht mit Thorium-X behandelt, *Wien. klin. Wehnschr.*, 1912, No. 25, ii, 1969. Increased Uric Acid Excretion after Radium. Mesernitsky, P., und Kemen, J.: Ueber Purinstoffwechsel bei Gichtkranken unter Radiumemanation-behandlung, *Therapie der Gegenwart*, 1910, N. F., xii, 526. Armstrong: Die Radiumbehandlung von Stoffwechselkrankheiten, 28 *Kongr. f. inn. Med.*, 1911, p. 148. Von Noorden, C. und Falta, W.: Klinische Beobachtungen über die physiologische und therapeutische Wirkung grosser Dosen von Radiumemanation, *Med. Klinik*, 1911, No. 7, ii, 1487. Kikkoji, T.: Ueber den Einfluss von Radiumemanation auf den Gesamtstoffwechsel im Organismus, *Radium in Biologie und Heilkunde*, 1911, i, 46. Mesernitsky, P.: Ueber die Schädigung des Organismus durch hohe Dosen von Radiumemanation, *Arch. f. physikal. Med.*, 1911-12, vi, 50.

⁴ Knaffl-Lenz, E. von, und Wiechowski, W.: Ueber die Wirkung von Radiumemanation auf Mononatriumurat, *Ztschr. f. physiol. Chem.*, 1912, lxxvii, 303.

⁵ Kerb, J., und Lazarus, P.: Zur Frage des Abbaues von Mononatriumurat unter dem Einfluss von Radiumemanation bezw. Radium D, *Biochem. Ztschr.*, 1912, xlii, 82.

⁶ Chase, A. F., and Fine, M. S.: The Use of Atophan and Radium Emanation in the Treatment of Gout and Arthritides, *Jour. Am. Med. Assn.*, 1914, lxxiii, 945. Fine and Chase: *Jour. Pharm. and Exp. Therap.*, 1914, vi, 219.

⁷ Mannes and Wellman: Klinische Erfahrungen in der Behandlung mit Radium Trink und Badekuren, *Ztschr. f. physik. und. Diät. Therapie*, 1910, xiv, 321. Umber in the discussion of Armstrong's paper: Die Radiumbehandlung von Stoffwechselkrankheiten, *Verhandl. de Kongr. f. inn. Med.*, 1911, 28, 48, see p. 177. Mandel, H.: Arthritis urica unter Radiumemanation, *Radium in Biologie und Heilkunde*, 1911, ii, 162. Kehrer: Neue Beobachtungen über die Wirkungsweise von Atophan und Radium im Purinstoffwechsel und deren Bedeutung f. Pathogenese, Diagnose, und Therapie der Gicht, *Arch. f. Verdauungskrank.*, 1913, 19. *Ergänzungsheft*, p. 98. Rosenbloom, F.: A Study of the Urinary Nitrogen and Sulphur Partition in a Case of Rheumatoid Arthritis Treated with Intravenous Injection of Radium Salts, *Am. Jour. Med. Sc.*, 1915, xlvii, 718.

infectious type; a woman, aged sixty-one years, with the hypertrophic type; a woman, aged sixty-five years, with the gouty type.⁸

These patients, who were on a purin-free, creatin-free diet, received, five times a day, 3 ounces of water impregnated with radium emanations, 20,000 Maché units in all. We measured the daily urinary output of uric acid, creatinin, nitrogen and water and the uric acid content of the blood before, during and after the treatment.⁹

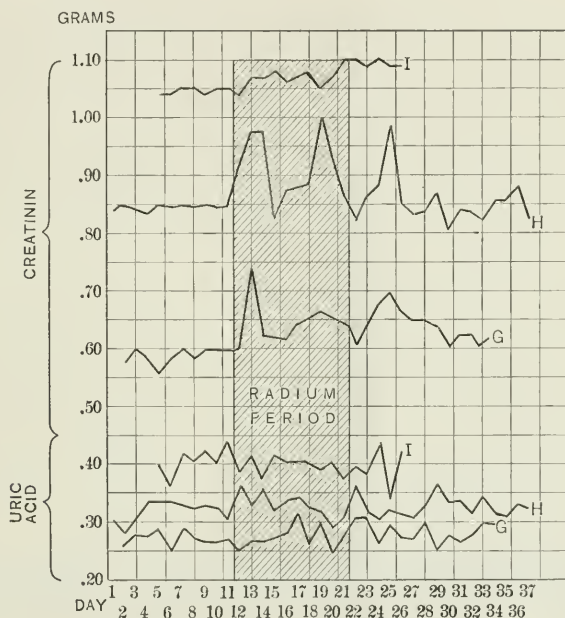
Day.	Hypertrophic arthritis.		Gout.		Chronic arthritis, infectious type.	
	Creatinin.	Uric acid.	Creatinin.	Uric acid.	Creatinin.	Uric acid.
	Preliminary period.		Preliminary period.		Preliminary period.	
1	0.839	0.308				
2	0.850	0.286	0.577	0.262		
3	0.847	0.307	0.611	0.280		
4	0.838	0.339	0.588	0.277		
5	0.849	0.335	0.559	0.287		
6	0.844	0.335	0.585	0.251	1.04	0.400
7	0.845	0.330	0.597	0.291	1.04	0.357
8	0.846	0.322	0.584	0.274	1.05	0.416
9	0.850	0.328	0.595	0.266	1.05	0.409
10	0.847	0.324	0.594	0.265	1.04	0.423
11	0.843	0.300	0.596	0.272	1.05	0.402
Ave.	0.845±0.003	0.320±0.014	0.523±0.016	0.266±0.016	1.045±0.005	0.401±0.015
	Radium period.		Radium period.		Radium period.	
12	0.930	0.362	0.606	0.252	1.05	0.441
13	0.977	0.324	0.740	0.270	1.04	0.386
14	0.975	0.356	0.621	0.269	1.07	0.419
15	0.824	0.320	0.617	0.272	1.07	0.374
16	0.872	0.338	0.617	0.280	1.08	0.414
17	0.880	0.341	0.645	0.313	1.06	0.404
18	0.881	0.324	0.651	0.262	1.07	0.409
19	0.999	0.318	0.664	0.296	1.08	0.400
20	0.929	0.291	0.655	0.245	1.05	0.390
21	0.861	0.310	0.648	0.279	1.07	0.403
Ave.	0.923±0.049	0.328±0.017	0.646±0.025	0.274±0.015	1.10	0.376
	After period.		After period.		After period.	
22	0.822	0.363	0.609	0.308	1.10	0.435
23	0.862	0.318	0.647	0.313	1.09	0.335
24	0.887	0.308	0.680	0.261	1.09	0.424
25	0.985	0.324	0.697	0.292	1.076±0.016	0.400±0.019
26	0.851	0.318	0.662	0.277	(Ave.)	(Ave.)
27	0.833	0.309	0.649	0.270		
28	0.836	0.331	0.650	0.299		
29	0.870	0.366	0.638	0.250		
30	0.803	0.334	0.606	0.277		
31	0.840	0.337	0.622	0.270		
32	0.837	0.316	0.621	0.274		
33	0.827	0.345	0.606	0.299		
34	0.858	0.318	0.620	0.298		
35	0.859	0.310				
36	0.880	0.332				
37	0.822	0.328				

Only one definite change in the metabolism was observed: A slight increase in the rate of creatinin excretion with a somewhat increased variation in the day-to-day values, an effect which per-

⁸ The clinical results of our studies of radium therapy are to be published separately.

⁹ Creatinin and uric acid analyses were made in duplicate by Folin's colorimetric methods.

sisted for a time after discontinuing the radium treatment. These changes, though slight, are, it will be noticed by comparison with the preliminary periods in each case, outside the limits of variation due to the analysis or to physiological variations. Objective evidence that improper collection of twenty-four-hour specimens is not responsible for the variation is afforded by the fact that the irregularities begin promptly with the radium treatment and are not, moreover, accompanied by similar variations in the uric acid excretion.



The above chart shows the daily excretion of uric acid and creatinin on three patients with chronic arthritis (*I*, infectious type; *H*, hypertrophic type; *G*, gouty type) for a period of thirty-seven days. From the twelfth to the twenty-first day radium water was administered.

The radium therapy had no influence on the uric acid content of the blood or on the rate of excretion of uric acid, total nitrogen or water.

We know, as yet, so little regarding the physiology of creatinin that a full interpretation of the increased creatinin elimination is not possible, but the data would appear to establish the physiological activity of radium water and to raise a considerable doubt that it has any influence on uric acid metabolism.

CONCERNING THE ANATOMY OF THE CORONARY ARTERIES.¹

BY FRED M. SMITH, M.D.,

ASSISTANT IN MEDICINE, RUSH MEDICAL COLLEGE, CHICAGO, ILLINOIS.

FOR some time I have been engaged with experiments on the coronary arteries of the dog. As a preliminary a study was made of the anatomy of those arteries, the special object being to compare their distribution in the dog and man. What is here described is a fragment of the work, which is very similar to the anatomical study of the coronaries made in 1907 by Jamin and Merkel. While chiefly confirmatory of what they and others have shown it varies somewhat in details and for this reason as well as for the inherent interest and importance of the subject it seems to warrant a brief report. First, however, let me recall some previous observations of others that have important bearing on the problems connected with the coronary arteries.

Cohnheim and Schulthess-Reichberg² reported, in 1881, the first observations on the coronary arteries that aroused much interest. In their extensive experimental work on curarized dogs both ventricles stopped in diastole within two minutes following the clamping of either of the main branches of the left coronary artery. They concluded that the coronaries were end-arteries, and if anastomosis did exist it was by means of very fine capillaries.

Erichsen³ had previously, in 1842, called attention to the relation of arteriosclerosis and angina pectoris. He was aware of the fact that in man the sudden occlusion of one of the large branches of the coronary arteries by a thrombus was a frequent cause of death, and he produced death experimentally in pithed dogs by the ligation of these vessels. Bezold and Breymann⁴ verified these observations in their work on curarized rabbits. Cohnheim's conclusions were soon doubted. Investigators took up the problem from the side of animal experimentation as well as from anatomical study. Fenaglio and Draugnell,⁵ in 1888, reported dogs which lived following the ligation of one of the large branches of the coronary arteries. Porter,⁶ in 1894, had still more favorable results. He had dogs which lived for days following the ligation of one or two of the large

¹ Read before the Chicago Society of Internal Medicine.

² Ueber die Folgen der Kranzarterienverschlussung f. das Herz, Virchows Arch. f. path. Anat., 1881, lxxxv, 503.

³ Influence of the Coronary Circulation on the Action of the Heart, London Med. Gaz., 1842, ii, 561.

⁴ Untersuchungen über die Herz und Gefassnerven der Saugthiere Untersuchungen a. d. physiol. Lab. zu Wurzburg, 1867, i, 256.

⁵ Cited by Herrick.

⁶ Results of Ligation of the Coronary Arteries, Jour. Physiol., 1894, xv, 121-138.

branches of the coronary arteries. Miller and Matthews,⁷ in 1909, further substantiated these observations. They reported a mortality of 8.7 per cent. following the ligation of the ramus circumflexus and no deaths following the ligation of the ramus descendens anterior of the left coronary artery as compared to Porter's results, who had a mortality of 88 per cent. following the ligation of the ramus descendens anterior. They concluded that the good results were due to the ether instead of curare and morphin as used by

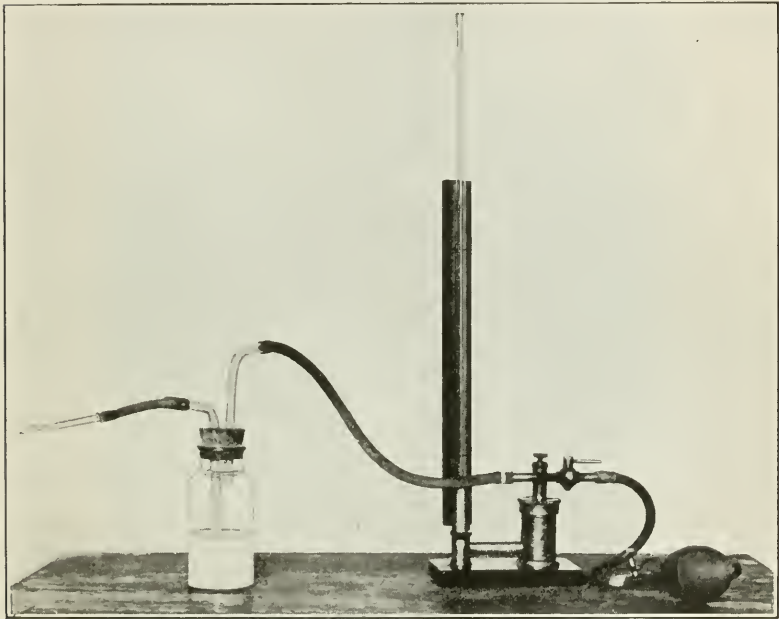


FIG. 1.—The apparatus used for injection of the coronary arteries.

Cohnheim, Fenaglio and Porter, and, furthermore, that there is an anastomosis between the branches of the right and left coronary arteries far greater than that suspected by Cohnheim.

Anatomical study threw still more light on the relationship of the coronary arteries. Amenomiya,⁸ in 1907, demonstrated by injection methods subpericardial anastomosis in the hearts of young individuals. Hirsch and Spalteholz,⁹ in the same year, showed an anastomosis of considerable size in the hearts made transparent following the injections of the coronaries with chrome yellow and

⁷ Effects on the Heart of Experimental Obstruction of the Left Coronary Artery, *Arch. Int. Med.*, 1909, iii, 476-481.

⁸ Ueber die Beziehungen zwischen Koronararterien und Papillarmuskel in Herzen, *Virchows Arch. f. path. Anat.*, 1910, cx, cix, 187.

⁹ Koronararterien und Herzmuskel: *Deutsch. med. Wehnschr.*, 1907, No. 20.

gelatin solution. Jamin and Markel¹⁰ drew similar conclusions from stereoscopic skiagrams of hearts in which the arteries had been injected with wax containing iodoform.

Further evidence in favor of an anastomosis between the terminal branches of the coronary arteries is advanced by numerous autopsy observations which shows that the heart is often able to withstand the obstruction of a coronary artery or a large branch. James B.



FIG. 2.—The skiagram of a dog's heart in which the coronary arteries were injected with the barium mixture.

Herrick,¹¹ in an article on "Coronary Obstruction," cites autopsied cases reported by Merkel, Doch, West and others, including one of his own, in which various parts of the coronary system had been occluded by thrombi. In each instance the findings were indicative of an old lesion.

For a more extensive review of the literature on the coronary arteries the reader is referred to Porter,¹² Amenomiya¹³ and Herrick.¹⁴

¹⁰ Die Koronararterien des Menschlichen, Herzen in Stereoskopischen Röntgenbildern, Jena, 1907.

¹¹ Clinical Features of Sudden Obstruction of the Coronary Arteries, Jour. Am. Med. Assn., 1912, ix, 2015-2026.

¹² Loc. cit.

¹³ Loc. cit.

¹⁴ Loc. cit.

In the study of the coronary arteries the following technic was used: The heart within its pericardial sac was placed in the ice-box for twenty-four hours following death, so that *rigor mortis* might disappear. Cannulas were then introduced into the coronaries at their opening into the aorta and the heart infused with normal salt at 37° C. by means of apparatus shown in Fig. 1. The infusion was continued at a pressure which rarely exceeded 100 mm. Hg. in the dog and 150 mm. Hg. in man until the salt solution returned practically clear.



FIG. 3.—The injected heart of a man with marked fibrous myocarditis and sclerosis of the coronary arteries.

Following the infusion the coronary arteries were injected with a mixture of 2 parts barium and 10 parts water, to which was added a small amount of tragacanth to hold the metallic substance in suspension. This was injected at a pressure of 100 to 125 mm. Hg. in the dog and 125 to 150 mm. Hg. in man. Stereoscopic pictures were taken as soon as possible following the injection.

OBSERVATIONS. One could follow the course of the arteries with great ease after they were injected with the white metallic substance. This afforded an excellent opportunity to compare the coronary distribution in man with that in the dog.

By this method thirty hearts from dogs and twenty from man were studied. In all instances the arterial distribution in the dog and

man corresponded very closely. This similarity was also shown by the stereoscopic skiagrams. This is of importance, as it strengthens one in the belief that experimental results on the coronary arteries of the dog might be expected to be analogous to those in man.

During this comparative study of the coronary arteries of man and the dog, certain observations were made having a bearing on the question of anastomosis. When the hearts were infused the salt solution injected into one coronary artery escaped, drop by drop, from the cannula in the other coronary artery freely enough, so that

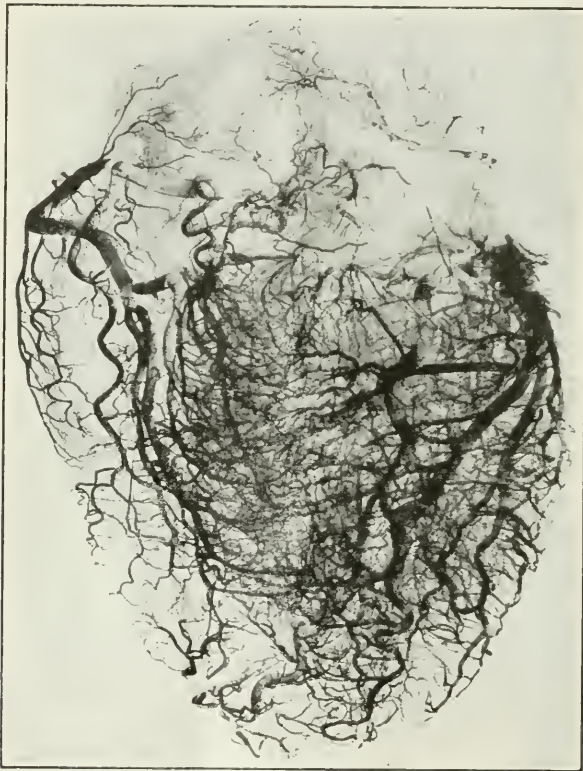


FIG. 4.—The injected heart of a young woman who died from pernicious anemia.

both arteries could be fairly well washed out by the infusion of one. This was noted both in the hearts of the dog and man. The salt solution could be seen entering the subpericardial distal branches of the ramus circumflexus sinister and the right coronary artery when injected into the ramus descendens sinister. I was also able to fill the distal branches of the right coronary and ramus circumflexus sinister with the barium mixture by injecting the ramus descendens anterior sinister with a pressure which did not exceed 100 to 125 mm. Hg. in the dog and 140 to 150 mm. Hg. in man.

The vascular richness of the cardiac muscle is perhaps better demonstrated by the stereoscopic skiagrams than by any other method. This vascularity seemed to be more marked in man than in the dog, as is shown in Figs. 2 and 4. These figures leave no doubt that there are anastomoses between the branches of the right and left coronary arteries. This is in most cases by means of many small vessels; only occasionally is one able to recognize an anastomosing vessel of any size.

This stereoscopic method shows nicely how the blood supply to the heart muscle may be markedly diminished by arteriosclerosis. Stereoscopic pictures were taken of hearts from patients varying in age from six months to sixty years. In some, which showed definite sclerosis of the aorta and coronary arteries, the number of small branches was markedly decreased, as shown by Fig. 3, from the heart of an old man showing marked fibrosis of the myocardium. In a case of this character it is easily understood how the occlusion of either of the larger branches by a thrombus would be more than likely to bring about death within a relatively short time. On the other hand the occlusion of one of the large branches shown in Fig. 4, where there is a rich network of unobstructed and anastomosing vessels, might, contrary to the view of some, particularly if the obstruction were gradual, be compatible with life.

CONCLUSION. 1. The distribution of the coronary arteries in the dog is practically the same as in man. Therefore, experimental studies of the coronary arteries in the dog will give a clearer conception of the pathology of these arteries in man.

2. There is an anastomosis between the branches of the right and left coronary arteries, which is, for the most part, by means of many small vessels, but distinctly numerous and large enough to functionate.

I wish to take this opportunity to express my appreciation to Dr. James B. Herrick for many helpful suggestions, to Dr. J. C. Rowntree, for his kindness in taking the skiagram and to the pathological departments of the Presbyterian and Cook County Hospitals.

FAT REDISTRIBUTION IN THE HYPOPHYSEAL TYPE OF DYSTROPHY ADIPOSEGENITALIS.¹

By HARVEY G. BECK, M.D.,

CLINICAL PROFESSOR OF MEDICINE, UNIVERSITY OF MARYLAND, SCHOOL OF
MEDICINE AND COLLEGE OF PHYSICIANS AND SURGEONS, BALTIMORE.

THE function of the pituitary, like that of the thyroid, presides largely over growths, development and metabolism. The gonads

¹ Presented at a meeting of the Baltimore City Medical Society as a part of a symposium on Disturbances of the Internal Secretions.

also have an important influence over growth and development, but perhaps somewhat less over metabolism. There is a close reciprocal function between these three glands which has been observed clinically and demonstrated experimentally.

Because of this reciprocal function, true hypophyseal fat dystrophies are rather rare. On the other hand the mixed or pluriglandular types are quite common. It is not uncommon to find in the same individual clinical evidence of hypothyroidism, hypopituitarism and hypogonadism in which the character of dystrophy varies, depending upon the relative insufficiency of the respective glands.

Although primary genital dystrophy occurs, it is relatively infrequent as compared with hypophyseal dystrophy. Moreover, the genital type usually early becomes a mixed type, in which hypophyseal symptoms predominate.

In the study of a large series of cases of hypothyroidism, fully 20 per cent. showed marked evidence of hypophyseal fat dystrophy, and practically all the female patients, which comprise nearly the whole group, gave a history of ovarian deficiency.

Disordered function of the pituitary gives rise to various types of dystrophy, depending on overfunctioning—hyperpituitarism; underfunctioning—hypopituitarism; or perverted functioning—dyspituitarism.

Gigantism and acromegaly are generally ascribed to a hyperfunction of the anterior lobe, although recently Roussey's doctrine, according to which it is due to dyspituitarism, has received many adherents. The dystrophies in these conditions are largely confined to cartilage and bone.

It is generally conceded that the fat dystrophies of pituitary origin, with which we are chiefly concerned in this paper, are due to hyposecretion of the posterior lobe. The most commonly recognized form is known as hypophyseal dystrophy adiposogenitalis—*typus Frölich*, by whom it was described in 1901.

The pathogenesis of *adiposis dolorosa*, or Dercum's disease, has not been definitely established, although it is undoubtedly a ductless glandular disease, possibly pluriglandular, in which the posterior lobe of the pituitary shares in a very large measure.

The adiposity that is frequently associated with acromegaly is thought to be due to secondary involvement of the posterior lobe.

My interest was awakened in the general subject of hypophyseal dystrophy in the summer of 1915, when I was consulted by two patients who presented the following clinical pictures: Case I was that of a woman, aged forty-one years, five feet three inches tall, weighing 125 pounds. She was married, but never pregnant. Her health had been good until eighteen months previous, when menstruation became irregular and the flow diminished until there was finally complete cessation.

During the ten months preceding the examination she had gained

about twenty pounds in weight. With this gain in weight she noticed an enormous increase in the circumference of the hips, upper thighs and abdomen, but there was no perceptible increase in the circumference of the thorax, neck and upper arms or any increase in the size of the face, forearms and hands or legs and feet. In fact, these parts had the appearance of one undernourished and emaciated

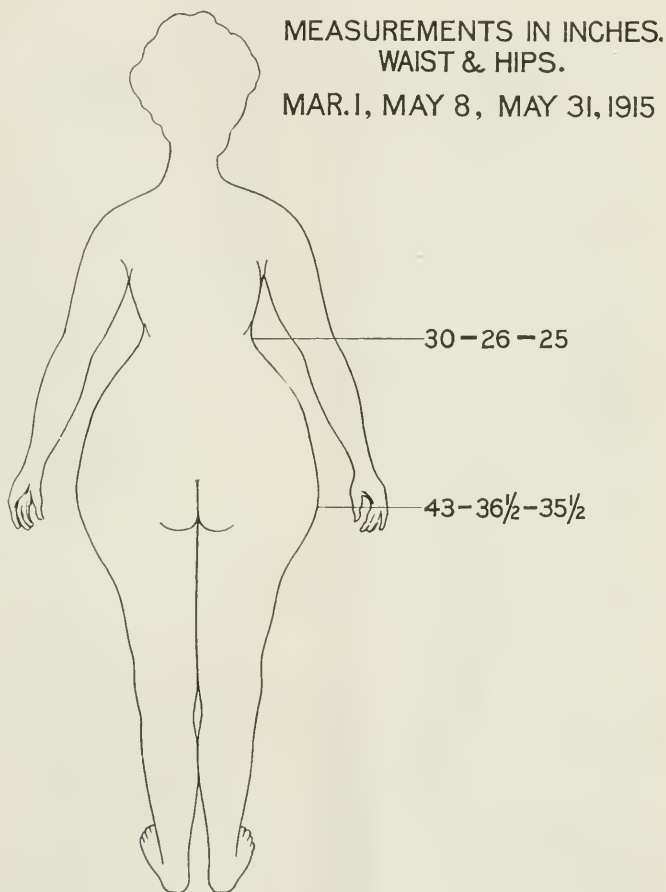


FIG. 1.—Illustrating the effects of organotherapy in dystrophy adiposogenitalis. Note the enormous reduction in hips and waist, with practically no loss in weight.

features, when contrasted with the extraordinarily large hips and abdomen for a woman of her size, presenting a striking abnormality in the configuration of her body.

In addition she suffered with apathy, stupor and dulness, impairment of memory, sluggish bodily movements and trophic disturbances of the skin and hair. She was a confirmed invalid and unable to

attend to ordinary household duties. Three fairly well-defined symptom groups were recognized in this case, namely, those referable to ovarian insufficiency—sterility and amenorrhea; those referable to pituitary insufficiency—abnormal character and distribution of fat; those referable to thyroid insufficiency—mental, neuromuscular and trophic skin disturbances.

On the basis of a pluriglandular syndrome, hormotone, which contains the substance of the three glands involved, was prescribed. Four tablets, with the addition of two grains of thyroid, were given daily. The results were very striking. The patient was speedily restored to normal mental and bodily vigor and was able to perform her usual domestic duties without the least fatigue; but the most remarkable effect of treatment was upon the fat dystrophy, the so-called dystrophia adiposogenitalis, as evidenced by a rapid diminution in the circumference of the hips and abdomen.

This rapid diminution necessitated her to resort to the free use of safety-pins to keep her clothes adjusted, and in the course of two months she had to have her clothing entirely refitted, although she had just purchased new apparel before she undertook treatment. At my request she procured the measurements as recorded by her seamstress, which are as follows:

March 1. Two weeks before treatment was begun: waist 30 inches, hips 43 inches.

May 8. After eight weeks' treatment: waist 26 inches, hips 36½ inches.

May 31. After eleven weeks' treatment: waist 25 inches, hips 35½ inches, a decrease of 5 inches in circumference at the waist and 7½ inches at the hips, with the loss of only one pound in weight (Fig. 1).

Thyroid was discontinued on June 14, but she continued to take four hormotone tablets daily until July 15, after which glandular therapy was discontinued. Since then, a period of two years, she has had no return of symptoms and retained her normal figure.

Case II, very similar in type, was a woman, aged forty-nine years, married, who weighed 148 pounds. Her general health was good until one year previous to examination, when she began to suffer with pain in the back, painful and frequent micturition, polyuria, headaches, emotional disturbances and mental depression. Her menstrual history was normal, although she was never pregnant. The most striking feature was her abnormal figure, in which the body from the waist down was relatively twice as large as from the waist up. Figs. 2 and 3, which were reproduced from photographs on an exact scale, will show the abnormal contour, due to deposits of fat over the lower abdomen and upper thighs, although the entire legs are involved in this trophic disturbance. A comparison between the size of the arms and legs will show this marked contrast. Her waist measurement was 69½ cm. and the hips 113 cm.

After one month's treatment with hormotone and anterior pituitary lobe (P., D. & Co.) she lost two and a half pounds in weight. Although no measurements were taken the patient stated that the circumference of her hips diminished so rapidly that she had to have her skirts reduced around the hips three times since the beginning of treatment and that her general condition had much improved.



FIG. 2



FIG. 3

Illustrating Case II.

The result of organotherapy in these two cases was as pronounced as it was mysterious. Although, according to both patients' statements, their busts had markedly developed, as well as the necks, arms and faces, yet there was no means of ascertaining, with any degree of accuracy, the extent of these alterations or the correctness of their statements. What actually became of the dystrophic fat was a

matter of conjecture and had to be determined by further study and observation. This was accomplished by the simple method of mensuration systematically employed in a series of similar cases while under treatment. The results clearly demonstrated that in a certain group, possibly 50 per cent., there is a redistribution of fat rather than a loss of fat.

On the other hand there is a group in which the fat dystrophy is not the least influenced by organotherapy. The most favorable cases apparently are those in which some chronic infection antedating the onset of symptoms is first removed.

Those cases following the menopause or operative procedures involving the thyroid or sexual glands do not seem to respond as readily.

Chronic focal infection and trauma through surgical intervention to some of the chain of ductless glands, especially the thyroid and sexual glands, are fairly constant factors in the history of patients suffering with dystrophy adiposogenitalis, and may have an important etiological significance.

In the literature no reference was found where measurements were used as a basis for determining the results of organotherapy; however, in the treatment of glandular fat dystrophies numerous examples of cases treated with various combinations of ductless glands were observed in which the weight was the sole factor of estimating the effect of this treatment.

The following is one of a series of twelve cases thus influenced to varying degrees by organotherapy:

CASE III.—Mrs. B., aged forty-two years; weight, 118 pounds. For six years she suffered with chronic appendicitis and spastic constipation. During the previous year she developed symptoms of hypothyroidism, with mental dulness, loss of memory, somnolence, muscular and joint pains, snapping joints, subnormal temperature and a sense of profound exhaustion. Recently she noticed that large cushions of fat were accumulating about her hips and upper thighs, and she was unable to wear her usual clothes. Her friends also noticed this tendency. This deposit of fat extended down to the middle of the thighs and was particularly prominent over the gluteal region and above the ilii, where large folds appeared over the lateral aspect of the abdomen, forming a large curved outline beginning at the waist and extending to the middle of the thighs. There was also a big fold of fat over the lower abdomen, with enlargement of the mons veneris, presenting a typical picture of dystrophy adiposogenitalis.

The treatment consisted of the removal of the appendix and administration of thyroid and anterior pituitary lobe (P., D. & Co.). Fig. 4 shows the remarkable influence of this treatment upon the shape of the body, while the general improvement compares very favorably with the restoration to her normal shape, with a gain of

three pounds in weight. After six months' treatment her weight was 124 pounds, axillary measurement $82\frac{1}{2}$ cm., waist 66 cm. and hips $96\frac{1}{4}$ cm.

Other cases of this type, similarly treated, have demonstrated the fact that the fat is redistributed and that the mere weight of the

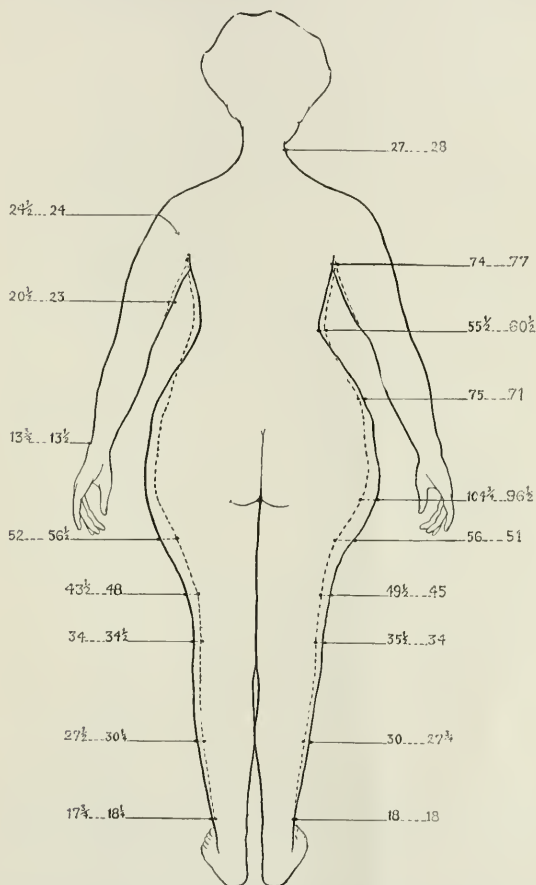


FIG. 4.—Illustrating Case III. Dark, continuous line and figures represent the body outline and circumference measurements recorded December 8, 1915. The dotted lines and figures represent the same recorded February 2, 1916.

patient is no criterion on which to base the results of treatment. The influence of organotherapy can best be determined by mensuration.

The preceding cases represent the more usual type of hypophyscal dystrophy. Occasionally one meets with certain variations from this type. For example, in the more advanced cases the fat dystrophy is more general and includes enlargement of the breasts,

with large scapular folds and cushions about the neck. However, the face, hands and forearms and feet and ankles usually escape.

There is a third group in which there is not only an increase in the accumulation of fat about the hips, buttocks, thighs and breasts, but in which there is also a unilateral increase. Three such cases occurred in my series. The following is an illustration:

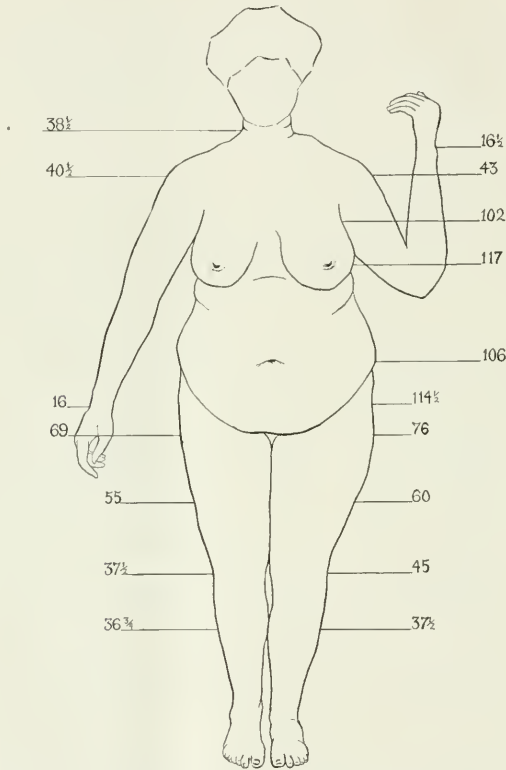


FIG. 5.—Illustrating Case IV. Note the disproportion of the measurements of the two sides.

CASE IV.—Mrs. V. B., aged twenty-four years. When married, three and a half years ago, she weighed 145 pounds. Since the birth of her child, two and a half years ago, her weight had increased rapidly, until she weighed 206 pounds. There is no obesity in the family. She had some well-marked symptoms of hypothyroidism, such as mental dulness, neuromuscular pains, Murray's hallucination, crunching joints, vesical irritability, etc., although the adiposity was not characteristic and the hair was oily, the skin moist and the fingers tapering. There was a relative increase in the deposition of fat on the left side, which could be readily discerned by inspec-

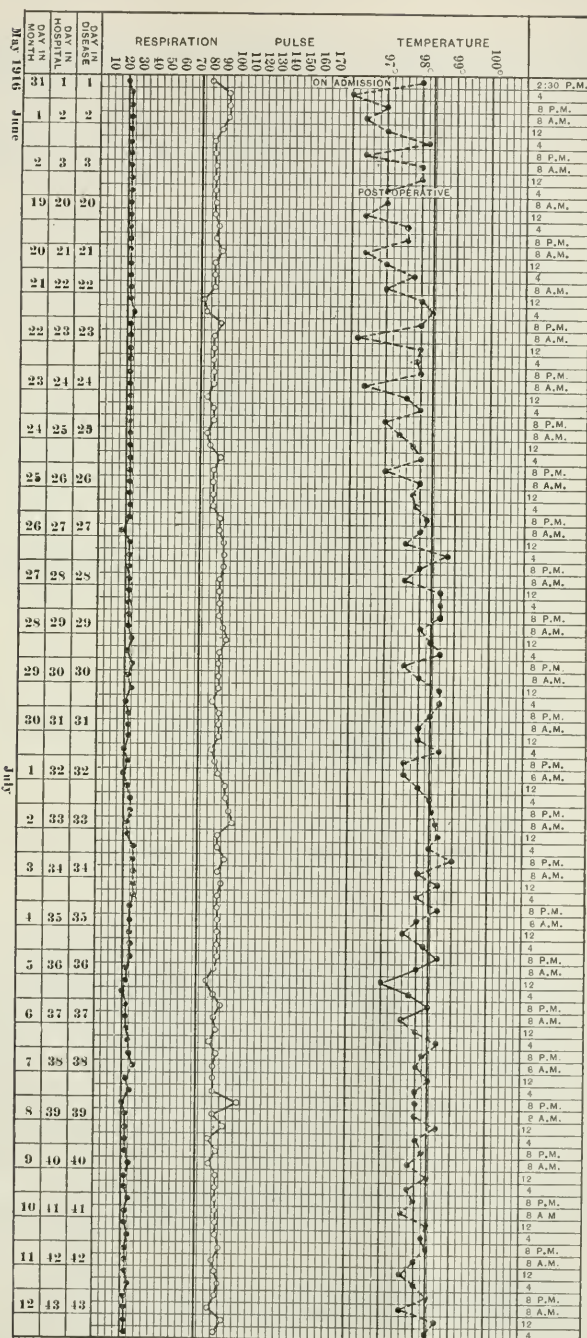


Fig. 6.—Chart of a patient suffering with hypophysal dystrophy, showing the effect on temperature of draining the antrum and administering thyroid and anterior pituitary lobe.

tion. There were cushions of fat over the upper dorsal region, extending over the shoulders; the breasts were large and pendulous, the left one larger than the right. There was a transverse cushion at the sulcus, formed by the umbilicus, and another at the ilium, which formed an apron, and still another between the umbilicus and the groin. Mensuration showed a hemidystrophy of fat, the left side being the larger (Fig. 5).

Unfortunately, this patient did not follow out any treatment. However, another patient of this type, treated since, showed a definite tendency of the measurements of the two sides to equalize. At the same time the umbilical and hip measurements decreased and the waist and axillary increased.

In conclusion, it is perhaps well to state that in none of the cases treated was any special attention paid to diet. The obesity is endogenous. The results may be attributed to the effect of the chemical stimulation of the cells by the hormones employed, thus favoring metabolism. The point to be emphasized is the fact that in certain cases of hypophysical dystrophy the fat is actually redistributed and that the only exact means of determining the effect of treatment is by some systematic method of recording measurements in addition to weight.

COMPLEMENT-FIXATION IN HODGKIN'S DISEASE AND ALLIED AFFECTIONS.

BY H. T. KRISTJANSON, A.B., M.D.,

PATHOLOGIST AND RESIDENT SURGEON TO MILWAUKEE COUNTY HOSPITAL;
ASSISTANT PROFESSOR OF CLINICAL SURGERY, MARQUETTE MEDICAL
SCHOOL, MILWAUKEE, WISCONSIN.

SINCE the report by Fraenkel and Much,¹ in 1910, of the all but constant presence of a Gram-positive non-acid-fast bacillus in the sediment obtained from glands in Hodgkin's disease, treated by their antiformin method, the most notable contributions to an etiological study of this disease are those of Negri and Mieremet² in Europe and Bunting and Yates³ in America. These workers, independently of each other, succeeded in obtaining, on special media, usually in pure culture, a non-acid-fast Gram-positive diphtheroid organism from the affected lymph glands in Hodgkin's disease.

Verploegh, Kehrer and von Hoogenhuzye,⁴ Billings and Rosenow,⁵

¹ Ztschr. f. Hyg., 1910, xlvii, 159.

² Centralbl. f. Bakteriol., 1913, xlviii, 292.

³ Cultural Results in Hodgkin's Disease, Arch. Int. Med., August, 1913, p. 236.

⁴ München. med. Wchnschr., 1914, lxi, 1158.

⁵ Etiology and Vaccine Treatment of Hodgkin's Disease, Jour. Am. Med. Assn., December 13, 1913, p. 2122.

Lanford,⁶ Rea and Falconer,⁷ Kusunoki,⁸ Fox,⁹ Joes,¹⁰ Caronia¹¹ and others report the findings of diphtheroid organisms in pure cultures from frank cases of Hodgkin's disease. The organism has also been found in glands from cases of lymphosarcoma,¹² pseudo-leukemia,¹³ lymphocytic leukemia,¹⁴ acute¹⁵ and chronic,¹⁶ myelogenous leukemia¹⁷ and in the spleens of Banti's disease.¹⁸ Though this type of organism has been found quite constantly in the related group of diseases (Hodgkin's disease, lymphocytic leukemia, pseudo-leukemia and Banti's disease), negative results are recorded, and similar if not identical strains have been recovered from a variety of pathological lesions¹⁹ and even from relatively normal lymph glands.²⁰ Progressive histological and hematological changes, similar to the earlier morbid processes noted in Hodgkin's disease and Banti's disease respectively develop in the glands and spleens of animals that we have repeatedly inoculated with suitable doses of these organisms.

Bordet and Gengou²¹ devised and reported in 1901 a method by which the probable disappearance or complete absorption of the complement in mixtures of bacteria and their respective amboceptors, to which was added fresh serum containing complement, was shown. Thus if to such a mixture, after it had stood for one hour, an emulsion of corpuscles and hemolytic amboceptor were added no hemolysis resulted, it was assumed that the presence of specific bacteriolytic immune bodies had so sensitized the bacteria that they were able to absorb the complement completely; hence, it would not activate the hemolytic amboceptor subsequently added. Wassermann and Bruch²² and others have made use of the complement-fixation phenomenon in demonstrating the presence of antibodies in different sera. These facts prompted me to undertake the present

⁶ Am. Jour. Trop. Dis. and Prevent. Med., 1914, ii, 191.

⁷ Arch. Int. Med., 1915, xv, 438.

⁸ Virchows Arch. f. path. Anat., 1914.

⁹ Studies in Diphtheroids, Arch. Int. Med., No. 3, xvi, 465.

¹⁰ Jour. Missouri State Med. Assn., 1915, xvii, 91.

¹¹ Pediatrics, 1915, xviii, 481.

¹² Bunting, C. H., and Yates, J. L.: Bacteriological Results in Chronic Leukemia and Pseudoleukemia, Johns Hopkins Hosp. Bull., November, 1915, No. 297, vol. xxvi.

¹³ Ibid.

¹⁴ Steele, A. E.: Corynebacterium Hodgkini in Lymphatic Leukemia and Hodgkin's Disease, Boston Med. and Surg. Jour., January 22, 1914.

¹⁵ Simon and Judd: Acute Lymphatic Leukemia, Jour. Am. Med. Assn., 1915, l xv, 2128.

¹⁶ Bunting, C. H., and Yates, J. L.: Bacteriological Results in Chronic Leukemia and Pseudoleukemia, Johns Hopkins Hosp. Bull., November, 1915, No. 297, vol. xxvi.

¹⁷ Dias: Myelogenous Leukemia, Brazil Medico, abstracted in Jour. Am., Med. Assn., 1915, l xv, 2128.

¹⁸ Yates, J. L., Bunting, C. H., and Kristjanson, H. T.: Etiology of Splenic Anemia or Banti's Disease, Jour. Am. Med. Assn., December 19, 1914, p. 2224.

¹⁹ Rosenow: Surg., Gynec. and Obst., 1915, xx, 403.

²⁰ Bloomfield: Arch. Int. Med., 1915, xvi, 197.

²¹ Ann. de l'inst. Pasteur, 1901.

²² Med. Klin., 1905.

study before Olitsky²³ had reported uniformly negative results with this complement-fixation test in 6 cases of Hodgkin's disease, 2 of lymphosarcoma, 1 of lymphatic leukemia in which the diagnosis had been established histologically and 1 of doubtful nature.

The organisms used by him for the preparation of the antigen apparently were not autogenous. It seems necessary to use autogenous organisms in the preparation of antigen for complement-fixation, as, according to Kolmer,²⁴ "recent researches in bacteriology tend to show that different strains of the same microorganism have particular, and more or less individual, pathogenic and sometimes biological characteristics, and it is reasonable to assume that the antibody will likewise show individual properties and a special affinity for its particular antigen."

By making "cross-fixation" experiments with other organisms—*Bacillus xerosis* and Hoffman's bacillus, *pseudodiphtheriæ*—Olitsky showed that the diphtheroid of Hodgkin's disease (*Bacillus hodgkini*) is not only a type distinct from those organisms but also that the sera of animals inoculated therewith will give positive complement-fixation results. In 2 cases of Hodgkin's disease Negri and Mieremet found complement-fixation negative. In 2 cases of Hodgkin's disease and 1 of Banti's disease Lanford obtained agglutination of the organism with the sera.

In preparing the bacterial antigens for my observations the following methods were employed: Antigen No. 1, polyvalent, was prepared by growing several strains of the diphtheroids on ascetic phosphate agar for six days. The growths were removed by adding a sufficient amount of normal saline (10 c.c.) to each tube to make a milky emulsion. This suspension was thoroughly shaken and heated at 60° C. for one and a half hours and then filtered through a sterile Berkefeld filter. The resulting filtrate was preserved with 0.5 per cent. phenol. Antigen No. 2, polyvalent, was made from different strains of the organism grown on Loeffler's blood serum for several days. The bacterial emulsion was heated and centrifuged at high speed in order to throw down the bacteria. The supernatant fluid was preserved in 0.5 per cent. phenol. Better results were obtained from this antigen than from No. 1, and it was used in titrating most of the sera.

In cases of Hodgkin's disease or allied affections the different strains of the diphtheroids used in the preparation of the antigens had been isolated from the lymph glands. These were all represented in the series tested for complement-fixation. However, there were a number of sera examined from cases whose organisms were not included in the strains used in making the antigens.

²³ Results of Complement-fixation Studies with the *Corynebacterium Hodgkini*, Jour. Am. Med. Assn., April 3, 1915, p. 1134.

²⁴ A Practical Text-book of Infection, Immunity and Specific Therapy, 1915, pp. 473-474.

Case No.	Complement-fixation.	Duration of disease.	Clinical diagnosis.	Bacteriological findings.	Pathological diagnosis.	Treatment.	Remarks.
1	+	3 years	Polyarthrits (chronic)	Diphtheroid	Lymphosarcoma type	Tonsillectomy; vaccine; immune serum	Example of definite type.
5	+	Few months	Hodgkin's disease	+	Hodgkin's disease	Tonsillectomy; x-ray	Blood negative; von Pirquet neg.; complicated with syphilitic infection.
11	+	8 years	Lymphangitis; adenitis	+	Lymphosarcoma type	x-ray; vaccine	Well.
16	+	2½ years	Hodgkin's disease	+	Lymphosarcoma type	Excisions; vaccine; x-ray; Coley's serum; immune ser.	Probable recovery after apparent hopeless involvement.
6	+	1½ years	Hodgkin's disease	+	Hodgkin's disease	Excision; x-ray; vaccine	Successful palliation for 1½ years; dead.
12	+	7 to 8 years	Tuberculosis	+	Combined Hodgkin's disease and tuberculosis	Excision; x-ray; hygiene	Probable recovery; blood now normal.
24	+	?	Banti's disease	?	Typical Banti's disease	None	Dead; cancer of uterus.
2	+	2½ years	Hodgkin's disease	+	Hodgkin's (cellular)	Excisions; x-ray; tonsillectomy; immune serum	Advanced disease; life prolonged 2½ years.
17	+	5 years	Hodgkin's disease	Diphtheroid (a strain)	Hodgkin's (cellular)	Excision; x-ray; vaccine; immune serum	Advanced disease; life prolonged.
15	+	Hodgkin's disease	Hodgkin's dis. (Dr. Ewing's)	x-ray; further treatment declined	Dead.
23	+	Hodgkin's disease	Hodgkin's dis. (Mayo Clinic)	Tonsillectomy; x-ray	Well.
8	-?	2 years	Hodgkin's disease	+	Lymphosarcoma type	Given "606," elsewhere	Edema of glottis; dead.
9	-?	6 years	Tuberculosis	0	Hodgkin's disease (early)	Tonsillectomy; x-ray	Blood positive; von Pirquet negative.
3	-	6 months	Lymphatic leukemia	0	Lymphogenous leuk. (acute)	Tonsillectomy; x-ray	Dermatitis of pruritus; dead.
4	-	Few months	Hodgkin's disease	0	Hodgkin's disease (early)	x-ray; immune serum	Well.
7	-	1 year	Mycosis fungoides	Diphtheroid (a strain)	Lymphosarcoma type	Tonsillectomy; x-ray	Well.
10	-	6 years	Tuberculosis	0	Hodgkin's disease (early)	Tonsillectomy; x-ray	Well.
13	-	Hodgkin's disease?	Hodgkin's dis. (Dr. Ewing's)		
14	-	Hodgkin's disease?	Hodgkin's dis. (Dr. Ewing's)		
18	-	Banti's disease	Diphtheroid	Typical Banti's disease	Splenectomy	Recovery.
19	-	Few weeks	Hodgkin's disease	Hodgkin's disease (acute)	Tonsillectomy; x-ray; immune serum	Hopeless type of process.
20	-	Few weeks	Tumor of left tonsil	Lymphosarcoma type	Tonsillectomy; x-ray; immune serum	Apparent recovery.
21	-	Hodgkin's disease	Hodgkin's dis. (Mayo Clinic)		
22	-	Hodgkin's disease	Hodgkin's dis. (Mayo Clinic)		

Each antigen was standardized by testing for its hemolytic property and found to be non-hemolytic. They were carefully titrated for their anticomplementary doses with fresh complement and known antishoop hemolytic system. These reagents were carefully titrated immediately before doing the test.

The immune sera used in testing for the antigenic dose were from horses, dogs and rabbits that had received repeated intravenous injections of the organism over variable periods in some of our experimental work. Very potent sera were thus obtained from these animals, some of which had become quite sick, with marked febrile reactions, particularly following the earlier injections. Apparently the organisms were distinctly pathogenic for these animals. Sera from normal horses and dogs were used in the negative controls, and all showed complete hemolysis with trial antigens. At no time did the antigenic unit in the actual test exceed one-fourth of the anticomplementary dose of 1 c.c. of antigen No. 2. Complete inhibition was obtained with 0.1 c.c. of the trial antigen and 0.2 c.c. of the immune serum. Two units of antigen and 0.1 c.c. to 0.2 c.c. of fresh clear inactivated (heated to 56° C. for one-half hour) unknown sera were used in the tests.

NOTE.—In order to eliminate any possible bias the specimens of sera were brought to the laboratory labelled by numbers only. Each series tested had the additional protection afforded by testing more than one specimen from several of the affected individuals as well as sera from normal individuals. To keep this factor constant, serum from the same normal individuals was provided for each of the different series.

Control antigens were prepared from the colon bacillus and typhoid bacillus. These gave negative results with the immune sera.

Thirty-two specimens of sera were examined from 24 cases. Of 16 cases of Hodgkin's disease, 3 (note), or 18 $\frac{3}{4}$ per cent., gave positive complement-fixation test, 4 doubtful and 9 negative.

In 1 case of combined Hodgkin's disease and tuberculous adenitis a slightly positive test was given. One case of polyarthritis associated with a diphtheroid infection gave a strong positive test at two different times. (These tests were made at the end of an acute exacerbation and in the beginning of a remission of the disease.) Two cases of Banti's disease were examined: one an advanced case, with cirrhosis of the liver, showed a slightly positive reaction (+ +); the other case, which had fully recovered from a splenectomy, done some time prior to the test, gave a negative finding. One case of chronic lymphocytic leukemia was negative. Two cases of lymphosarcoma type gave negative reactions. Three different specimens of serum from an individual whose affection histologically, hematologically and bacteriologically belongs to this group of diseases, were titrated. One specimen collected at the end of an acute exacerbation gave a moderately positive reaction (+ +); the other

two specimens, taken during a period of remission of disease, were negative.

NOTE.—One of these, an advanced case, was apparently in an aggressive phase of the disease when the test was made. Unfortunately, I was unable to ascertain exactly what stage of the disease the other two were in at the time of collecting the specimens. One of them, however, is progressing very favorably and is now apparently well.

As negative controls, sera from normal individuals²⁵ and from cases of tuberculosis, syphilis, etc.,²⁶ were examined in the same manner as the unknown sera, and all gave negative results. Olitsky tested thirty-four patients not suffering from Hodgkin's disease, with negative results.

It is essential that each patient should be tested for complement-fixation, not alone during the period of remission, but more particularly at or just after the height of an aggressive phase of the disease,²⁷ and with bacterial antigens prepared from an organism isolated from the diseased gland of the individual. One of our cases (No. 11) indicated the importance of this procedure. It is not only conceivable but indeed quite possible that the antibodies thrown into the body fluids during an aggressive stage may quickly disappear from the blood after the acute symptoms of the disease have subsided, and the serum may therefore give at other intervals a negative complement-fixation test even with a specific antigen. In this connection it should be borne in mind that as the disease progresses toward the terminal stage, even though the clinical manifestations of the period of aggression be more distinctly manifest, the evidence of a subsequent beneficial physiological reaction in local and general improvement is less pronounced. This may indicate that in advanced cases positive complement-fixation test might be constantly negative.

CONCLUSIONS. 1. Complement-fixation test in Hodgkin's disease, using the *Bacillus hodgkini*, preferably an autogenous culture, in the preparation of antigens, may give a positive, possibly a specific, reaction if the serum be obtained from the individual at the proper phase or stage of the disease.

2. Experimentally, animals inoculated with the *Bacillus hodgkini* give a specific positive complement-fixation.

3. Normal individuals and those suffering from syphilis and tuberculosis have not given this reaction in the limited number tested.

I am greatly indebted to Dr. J. L. Yates, for the clinical data and for obtaining most of the specimens of blood; to Dr. C. H. Bunting, for supplying many of the bacterial strains; and particularly to Dr. F. A. McJunkin, of Marquette University, and Dr. P. F. Clark, of the University of Wisconsin, for their assistance in the preparation of the bacterial antigens.

²⁵ Lanford: *Am. Jour. Trop. Dis. and Prevent. Med.*, 1914, ii, 191.

²⁶ Rhea and Falconer: *Arch. Int. Med.*, 1915, xv, 438.

²⁷ Yates: *Johns Hopkins Hosp. Bull.*, 1914, xxv, 180.

WAR MEDICINE

CONTRIBUTORS

- LIEUTENANT-COLONEL SIMON FLEXNER, M.C., U.S.A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U. S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- MAJOR RICHARD M. PEARCE, M.C., U.S. A., National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, M.C., U.S.A.
- MAJOR R. M. YERKES, Sanitary Corps, U.S.A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- MAJOR E. E. SOUTHARD, W.S., U.S.A., Director of Psychopathic Department, Boston State Hospital.
- COLONEL WARFIELD T. LONGCOPE, M.C., U.S.A. (Prof. Practice of Medicine, Columbia University).
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- COLONEL FREDERICK F. RUSSELL, M.C., U.S.A.
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- MAJOR A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- MAJOR O. H. PERRY PEPPER, M.C., U.S.A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Professor of Pediatrics, University of California).
- MAJOR FRED H. ALBEE, M.C., Director of Military Reconstruction Hospital No. 3, U.S.A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.C., U.S.A.
- MAJOR JOHN A. HARTWELL, M.C., U.S.A., Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- CAPTAIN RALPH PEMBERTON, M.C., U.S.A.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

HYPERTHYROIDISM IN THE RECRUIT.¹

BY MAJOR HARLOW BROOKS, M.C.,

CHIEF MEDICAL SERVICE AT THE BASE HOSPITAL, CAMP UPTON, L. I.

HYPERTHYROIDISM is a condition which in civil life I have previously considered as almost exclusively a disease of women, and particularly of rather unstable women, in their youth. One of the greatest medical surprises to which I have been treated since on active service has been the large number of cases of this type which have come under my observation as a member of the Cardiovascular Board of the Seventy-seventh Division and in the medical wards of our base hospital.

It is perfectly true that my conclusions in regard to the true nature

¹ Presented at open session of New York Academy of Medicine, February 12, 1918.

of this condition are open to question if one takes too seriously the title of my paper. The British have described precisely the same condition as I present under the heading of "The Effort Syndrome," or as "D. A. H.," which is real army English for disordered action of the heart. I have read many of their most excellent studies and have received from old students and friends serving with the British colors descriptions of their cases, and I have tried to consider with an open mind the whole complex problem. This group of circulatory phenomena forms an important and inseparable part of that still more uncertain condition known as "shell shock," and it occurs in many people who not only have never heard the song of the shell but particularly among many of those who most earnestly desire never to do so.

The material which has come to me in the past five months has been so abundant, so absorbingly interesting, that I frankly confess that thus far I have had neither sufficient time nor ability to properly digest the subject; as a would-be "good soldier," many other problems have put most insistent demands on my time, interests and sympathy; but in spite of these I am anxious to at least present my viewpoint of this most important and serious problem in order that you may assist us in working out the most important circulatory problem which the war has thus far presented and one of the most frequent disqualifying factors of otherwise available soldier material.

Please do not consider me so egotistic as to consider for one moment that what seems to me the very natural conclusion that this group of symptoms is due to hyperthyroidism is solely my discovery; quite the contrary, for I believe it to be the prevailing opinion in regard to the problem which is accepted among clinicians in active service, although many, and notably the British authorities, who have had exceptional opportunities for the study of this picture, are induced to ascribe it as due to infection or to unknown agents which are but vaguely hinted at.

The most striking feature of these cases in nearly every instance is tachycardia. This is the sign because of which most of the cases report to the regimental medical officer or on which they apply for exemption or discharge. It is constant in practically all examples of the syndrome, though it varies very greatly in degree. It is present alike in recruits presenting themselves for initial examination, in those who report later, and after considerable drill and army routine may have further served to upset the mental emotional and circulatory equilibrium of these patients.

The tachycardia is rarely accompanied by arrhythmia even in cases of very marked degree, and polygraphic studies, except in instances complicated by other vascular conditions, show, aside from rapidity, few signs of abnormal action, except that in the same case there is under varying conditions usually great variation in the rate of systoles. Practically always the rate is increased by exercise,

though there are exceptional cases in which, as in ordinary palpitation, exercise may slow the rate, especially when the attention is thereby distracted; but speed of action is even more constantly accelerated by excitement and disturbing emotional factors.

Closely associated with tachycardia is an obvious and subjective throbbing of the superficial vessels, notably of the carotids, of the brachials and even of the femorals, while that of the aorta, in moderately thin persons, is also quite evident. Naturally, in polygrams this throbbing of the vessels is very striking, and we have found this graphic method often the most secure way of differentiating this condition from the throbbing vessels of an aortic incompetence. Under excitement, instead of an increase in systolic stroke, there is a fall in the stroking power, and this is, as our tracings show, much more evident in the medium-sized vessels, as the smaller ones seem to contract while the larger vessels expand in their arc of pulsation. Naturally, with these symptoms and signs, there is a wide area of apical pulsation, and so violent is this at times that an actual sucking sensation is produced on the palpating palm at the diastole.

The heart sounds, because of their rapidity, are usually very difficult to analyze, but in a good many cases a soft systolic murmur is detected at the apex, and is transmitted at times with decreasing intensity toward the axilla. The marked alteration in the quality and occurrence of this murmur in the same case at different times is occasionally a striking diagnostic feature. Everything in the nature of graphic methods seems to indicate that these murmurs are functional and not organic in origin.

With these striking signs of circulatory derangement are many symptoms apparently secondarily consequent to the tachycardia. The capillary return is almost always much delayed. I have never seen a real capillary pulse in pure cases, but it is often closely simulated. Patients complain bitterly of an oppressive, and occasionally bursting pain in the region of the heart, and though doubtless many of them exaggerate the degree, one is very often able to demonstrate areas of hyperesthesia; that is, the head cardiac zones which the British authorities believe to be an important diagnostic feature of the disease. The pain is sometimes reflected into the left or right arm and shoulder as in angina pectoris. Sudden and rapidly succeeding flushing and paling of the face and upper thorax occurs as seen in ordinary exophthalmic goitre so commonly present in neurotic young women. The blood-pressure is very low, as is usually the case in tachycardia, except in hypertensive cases, and there is a notably low pulse-pressure in most instances. As has been shown by the various members of the British Cardiovascular Board, adrenalin causes an increase of the symptoms, and in my experience, which differs from that reported by the British, there is also apparently a hypersensibility to thyroid, though I have not pursued this investigation very far

because of its evident danger. The nitrites markedly increase the symptoms and there is a general hypersensibility to the vasomotor dilators.

This symptom of tachycardia is not controlled by digitalis even when given in massive doses. The sedatives at times, notably the bromides, give marked relief in some instances, but are apparently without effect in others. Postural and emotional rest appear to be the most efficient measures of control. Cold applications to the precordium have little or no effect. Very closely associated with these definitely circulatory symptoms are those of dizziness and fainting. Commonly these attacks are accompanied either by a marked paling of the face or by a marked hyperemia. Such attacks are directly precipitated by exercise or by emotional stress, such as, for example, occurs during a physical examination. Next to the tachycardia the manifestations which seem most striking to me are numerous evidences of emotional instability, which is an invariable accompaniment of the disease. In some few subjects there is an effort to suppress these symptoms, but once the confidence of the patient is obtained or the barrier of reserve broken through the emotional temperament breaks forth, sometimes in epileptoid attacks, in bursts of passion, in tears, profanity or perhaps in convulsive muscular spasms.

Irritability of temper, headaches and insomnia are almost constant, and during aggressive periods an intense feeling of fear, apprehension and terror, often quite beyond the control of the patient, is manifest. Outbursts of emotionalism are followed by a stage of great exhaustion, almost amounting to prostration, in which the patient may appear to be *in extremis*. The palms of the hands and the soles of the feet become bathed in a copious perspiration, which is stone cold; local asphyxiae, as in Raynaud's disease, appear and may persist for some time. They are rarely bilateral. Sometimes exhaustion appears suddenly and without apparent cause, in other instances it follows only mental, emotional or physical effort. The neurovascular instability is further shown by the *tâche cérébrale*, by dermatographia, by urticarial rashes and by the almost constant symptom of tremor. This tremor is most marked ordinarily in the hands; it is fine, increased by intention, and though it occurs on both sides is very rarely synchronous or bilaterally equal. The very types of nationalities chiefly affected in this syndrome is a certain index of the strong emotional element in the disease. The Hebrews lead in over 50 per cent. of the numbers which have come under my observation, the Italians next, then the Irish, least of all is it seen in the negroes, among whom in about 5000 recruits I have observed but a single case, and that questionable.

Breathlessness at times, almost a dyspnea, is manifest, but without cyanosis or definite signs of asphyxia; they complain of great difficulty in breathing and of fear of suffocation; but deep inspiration

is possible if they can be induced to attempt it. Probably allied to the circulatory symptoms are small variations in temperature. Occasionally the temperature (mouth) will reach as high as 100° F., but usually not more than 99° F. Again, a subnormal temperature may be found. Usually the surface of the body is cold, especially the hands and feet.

The deep reflexes are excited, especially the knee-jerks. Most of these patients are above the average in mental acuity, and it is lamentably frequent among promising material for non-commissioned officers, though doubtless seen most frequently of all in those persons, whether blameworthy or not, who are struck with terror at the idea of active service and many of whom are keenly desirous of avoiding it. It is of course a difficult matter in many instances of this kind to unravel the real from the imaginary or assumed and to prevent successful malingering, especially when the tachycardia is accentuated by the use of atropin or of other drugs such as tobacco. Curiously, I have found this method, the employment of tobacco for attempted evasion of service, mentioned by many of the older authors on military medicine; it is a time-honored and still popular procedure.

To return again to the physical signs of the disturbance: I have mentioned the tachycardia, with the throbbing of the superficial vessels, the neurovascular instability, the tremors and the emotionalism, manifested, as you will note in the plates, by the worried and apprehensive facial expression of the patients, oftentimes so characteristic that my artist, not a medical man, when sent into a ward has usually been able to promptly select the patient whom he had been summoned to sketch. In about two-thirds of the cases one sees a very definite thyroid hypertrophy or at least a prominence of the thyroid. In some instances this amounts to an actual goitre, and this has been very evident in nearly all the cases which have been under observation for several months or which give a history of some time standing. It is of course well recognized that the size of the goitre or its lack of size is no measure of the activity of thyroid secretion, but the fact that in the long-standing case goitre is a most marked and almost constant symptom is indeed striking. The goitre may be symmetrical, it may chiefly involve the isthmus, one or both lobes, or it may be entirely symmetrical. Whether or not it is to be connected with the sign or goitre, or not, nearly all the cases complain bitterly of a choking sensation and of constriction of the throat, though they but rarely describe a typical globus hystericus.

A very interesting factor notable in most of these cases, and of very direct bearing on the question of the role which hyperthyroidism plays in this condition, is the certain part which heredity plays in the syndrome. A considerable number of cases give a history of ancestral goitre, particularly on the maternal side and sisters, less commonly brothers of the patients commonly show similar goitre.

There is also, in most instances, a familial history of nervous instability of hysteria, insanity perversions or of genius.

Exophthalmos, which is so striking a feature of ordinary exophthalmic goitre, as we see it so commonly in women, is present also in long-standing instances of this type. Not infrequently it develops very suddenly: it may be bilateral or monolateral or it may vary in either eye. During periods of excitement it is of course most evident, and as the tachycardia and emotionalism subside so also does the exophthalmos. I have seen, however, but a few cases which showed in any typical degree either von Graefe's or Stellwag's signs, but nearly all, especially in the more active instances, show more or less reddening of the conjunctivæ, with a desiccation of the membrane and complain of a strained sensation of the eyes.

Thus it will be seen that these cases present, though in perhaps mild degree in some instances, all the cardiac signs and symptoms of true Basedow's disease or exophthalmic goitre. Hence my assumption which I believe justifies the title that I have given my paper.

These patients endure the acute infections very badly; simple catarrhal colds, bronchitis and slight surgical incidents are all very poorly tolerated, while pneumonia, measles, scarlet fever and the like are much more serious in them than in others. Tobacco also apparently produces in them much more serious symptoms than in the average; so evident is this that most patients voluntarily give it up, confessing that it causes or increases cardiac pain, breathlessness, nervousness and dyspnea.

We also have noted, what has particularly impressed the British observers—namely, a distaste of these patients for alcohol. This is manifest even in those previously long accustomed to the use and appreciation of alcoholic drinks. Almost without exception they are rapid and large eaters, as Janney has shown to be the natural condition in persons suffering with hyperthyroidism.

Rest is the one factor which relieves these cases in my experience. Physical rest I would place as the most potent factor and mental or emotional rest as the second. This in either instance may be accentuated by the use of bromides or the more powerful sedatives.

Assuming that our inference as to the real nature of this striking clinical picture is correct, how are we to explain the appearance of so many of these cases among the young men of the draft age, whereas it has been so uncommonly observed at other times? Why are we civilians, suddenly forced into military medicine, now for the first time seeing so many of these cases in the very people whom we have been largely handling in the past? The causes appear to me to be several, but yet very definite and logical in their action.

The role which emotional shock, fright or mental traumatism plays in the activation or evolution of Graves's disease is too well established to admit of question. Our knowledge in this respect of the hyperaction of the endocrines has been much amplified by

the researches of Cannon and Crile, especially in their relation to shock and fright. The young recruits called, often unwillingly, to the Colors is frightened to a degree often beyond the understanding of many of us; for weeks or months he has been worrying and worried over what must take place. For days he has been subjected to the sentimental and nervous stress incident to his separation from his family, and he has had to bear with the emotional explosions of his female relatives, especially if of those races in whom a certain melancholy and dramatic pleasure is taken in occasions of this kind. If any of you have viewed the separations which are inflicted on many young recruits, as I have frequently seen them in the Pennsylvania Station, you may perhaps faintly realize the shock to the nervous system which the ordeal implies and the great demand which is put upon the endocrine of the young recruit as a result.

This is much exaggerated of course if a very definite unwillingness to serve exists, but I would not for one moment have you assume that it is in only such that these cases appear. One of the most definite cases which I have seen was in the person of a very brilliant Italian clergyman, but recently graduated, who nearly fainted when he found that because of his tachycardia it was unlikely that he would be accepted, and who finally, when his urgings and protestations had secured from us the privilege of a trial, ran back to his barracks shouting like a Bersagliera at the charge.

Add to this the sexual excesses in which the young recruit often indulges before his call comes, the excesses in eating and in that last good-bye drunk and a series of conditions calling out to the superlative degree, activity on the part of the thyroids is presented which could act only in the manner detailed.

The early days spent in the cantonment serve to more accentuate these conditions. He is forced into a new and strange life, new acquaintances surround him, all also in a state of mental and physical unrest. The heavy strain of the physical examination, the newness and severity of the setting-up drill dominating and pervading it all, and oftentimes intense nostalgia, and that a tendency toward the condition should become accentuated is but to be expected.

The question of treatment of this condition is a matter which I do not wish to consider at this time for the reason that I do not feel that as yet I have a sufficient experience in this matter to speak with personal authority. Thus far with us it has been chiefly the question as to whether or not these subjects have the making of soldiers in them. Many of the cases recover under the really healthy and normal routine life of the military camp; this is particularly likely to be the case with those who are happy in their work or in whom the sense of duty and obligation overrule a natural timidity and sense of fear. If in these persons a careful training is imposed, not too severe

until the recruit is prepared for heavy work, if the worry and strain is sufficiently relieved by reaction, games and camp shows, these men, oftentimes of the finest spiritual and patriotic fiber, are certain to make good soldiers, competent and spiritually equal to great and heroic deeds; but if, on the other hand, unhappiness comes or overly heavy or premature physical work are imposed, and perhaps the ridicule or worse of men of more rugged or phlegmatic temperament keeps the young soldier in a condition or a state of unhappiness and fear, he breaks either nervously or cardiac incompetence ultimately develops. This I have also seen in ambitious young men of the higher, more spiritual type who have at once striven to excel in their work and studies and to whom rapid advancement has meant unprepared-for responsibilities and worries.

The subject is an important one to us all at this time. It has been a most astonishing revelation to me, and I think to most civilian physicians who have been called into active service, and I feel that earnest study with a liberal adaptation of the excellent suggestions which have been worked out by our more experienced allies will permit us to salvage a considerable and very valuable human material which we will doubtless sorely need before many of us are able to lay aside our uniforms and return to our homes and the normal life which we all crave to such a degree that we are happy to fight for it.

EFFECTS OF "MUSTARD GAS" ON THE EYES.

BY GEORGE S. DERBY, M.D.,

MAJOR, M.O.R.C., U. S. A., NO. 13, GENERAL HOSPITAL, B. E. F.; U. S. ARMY
BASE HOSPITAL NO. 5.

LACRIMATORY gas was first used by the Germans to disable their opponents temporarily at the time of an attack. Its effects wore off very quickly and no harmful results remained.

In July, 1917, U. S. Army Base Hospital No. 5 and other hospitals in the vicinity began to receive a large number of cases poisoned by a new sort of gas which produced lesions of the eyes, the respiratory system and the skin. Since that time we have had perhaps 500 of these cases to treat.

Mustard gas is not sent over in clouds but in shells and its action is a delayed one, as it vaporizes slowly. It will hang around a locality in which it has been sent over for many hours. As this gas produces inflammation of the eyes in at least 80 per cent. of cases it is important that our medical officers should be able to recognize and to treat the ordinary case, and that our ophthalmologists who are coming over here should be well informed and prepared to help

their medical and surgical confrères when asked for advice, and asked they frequently will be.

In these notes I propose to confine myself chiefly to the ocular effects of the so-called mustard gas.

Dichlorethylsulphide, popularly known as mustard gas, is a dark brown liquid which vaporizes slowly. It has a faint but fairly distinctive odor, easy to recognize but hard to describe. It works best in the presence of moisture, and therefore it affects most the mucous membranes and the moist portions of the skin, the axillary folds and the genitalia. A well-constructed gas mask is impervious to its fumes, but naturally will not prevent the skin lesions.

The direct effects of mustard gas are usually not immediate, but are delayed for from three to eight hours. The soldier vomits, his eyes begin to burn and water and the lids often swell. The respiratory passages are very irritable and severe attacks of coughing come on. The skin lesions are seen later and vary in severity from a mild erythema to marked development of bullæ on the affected parts.

Many cases are gassed so mildly that they may return to duty in a few days and are not sent down to the Base. A large number, however, must be sent down and are kept in the Base Hospitals for a period varying from one to four weeks. They are then (in the British service) sent on to a convalescent camp and after a stay there of perhaps the same length of time they may be returned to their military base and so on back to their unit. The mortality is in the neighborhood of 2 per cent. and the commonest cause of death is bronchopneumonia.

OCULAR LESIONS. As mentioned before, some 80 per cent. of the cases we have received show eye lesions of greater or less severity. The lesions are of the nature of a chemical burn of the skin of the lids, conjunctivæ and of the corneæ in a considerable percentage.

THE LIDS. The picture presented by the patient whose eyes are severely affected is sufficiently striking. The lids are reddened, swollen and often show numerous large bullæ; they are kept tightly closed. The French speak of a true ulceration of the lid margin occurring most often in cases of pneumonia. This we have not observed.

The irritation and photophobia are so intense that not infrequently resort must be had to one or two drops of cocain and the use of a lid elevator in order to make a proper examination of the eye. Separation of the lids is often followed by a gush of tears.

The appearance of the conjunctivæ varies with the severity of the case. In the milder ones there is but slight injection, nearly always accompanied by slight photophobia. In the more severe cases we get a severe injection and at times a very marked white edema and chemosis of the membranes. These appearances are usually most marked in the area of the palpebral fissure. A secondary infection of the conjunctiva following gassing is not at all uncom-

mon. Ciliary injection is frequent. In the more severe gas cases a careful examination, made with proper illumination and the corneal loupe, will nearly always disclose a certain amount of corneal involvement, varying from a slight roughening of the epithelium to a well-defined opacity, usually in the form of a band extending across the cornea in the area corresponding to the palpebral fissure. In appearance this band in certain instances may assume an almost porcelain whiteness, but this is rare.¹

The French speak of ulceration of the corneæ as being common. In our experience it is rare. Personally, I have seen but three cases with a definite loss of substance. The first of these died about two weeks after being gassed, the second could not be followed, as he was evacuated to England. The third was transferred to the principal British eye hospital after being for ten days in another hospital. This case showed a severe central corneal ulceration with hypopyon. In spite of a Saemisch section the condition progressed and the eye was lost. Our British colleagues have seen a few corneal ulcerations, also usually of rather a mild type.

According to the French these corneal lesions are stained by fluorescein. In our experience they are not except in rare instances.

The corneal condition tends to disappear rapidly, leaving no trace, except in the cases with ulceration.

As a result of the corneal irritation one often gets a small pupil which may require the use of atropin three or four times a day to secure a satisfactory dilatation. In most instances, however, a drop of a 1 per cent. solution twice a day will act sufficiently.

Some observers have tried to make more or less of a mystery of the intense photophobia which occurs so frequently. This may quite certainly be explained by the corneal involvement.

Tellières has described a neuroretinitis characterized by a peculiar slate color. Fundus observations through a cloudy cornea are, however, difficult, and his findings have not been confirmed.

PROGNOSIS. Cerisé in his report to the Société d'Ophthalmologie divides these cases into three groups:

1. Benign: Representing 10 to 15 per cent. of cases. Duration ten to fifteen days.

2. Medium: About 80 per cent. of cases. Duration five or six weeks.

3. Severe: 3 to 5 per cent. seen in those with marked general symptoms, who often develop a bronchopneumonia.

Our experience would tend to put a larger proportion of cases in the benign class.

Although not possible to quote figures it may be said, speaking entirely from the ocular standpoint, that nearly a third of the cases

¹ Probably in these cases some of the fluid has come into direct contact with the cornea.

may be discharged to duty in a week and that a third more may go back by the end of the second week. In perhaps a fifth of the cases the duration is three or four weeks and the small remainder run a course up to two months. With very rare exceptions complete recovery results.

Men who are subject to blepharitis and conjunctivitis are more sensitive to gas.

Following exposure to mustard gas one sees a considerable number of patients, mostly those of unstable nervous system, who complain of photophobia and blepharospasm of a functional nature. The ocular membranes in these cases are normal or show at most a slight hyperemia. Such cases should, after a careful examination, be treated as purely functional treatment.

TREATMENT. Mustard gas burns of the eye, although tending toward spontaneous recovery, deserve careful supervision and treatment, since good treatment will shorten their convalescence, make them much more comfortable and ensure a complete recovery, except perhaps in the rarest instances.

The eyes should be protected from light but not bandaged. The patient should be kept in a moderately shaded ward. Eye shades which are satisfactory can be made out of three or four thicknesses of the blue paper in which various hospital supplies are wrapped.

The eyes should be gently irrigated in severe cases every three or four hours with some bland solution. Normal saline, soda bicarbonate 1 per cent., or boric acid are all good, best heated to about 100° F. before using. Following this a drop of liquid paraffin may be instilled or in the later stages argyrol in a 25 per cent. solution is found to be soothing. Castor oil theoretically is good, as mustard gas is dissolved by animal and vegetable but not by mineral oils. In practice, however, it is found to be more irritating than liquid paraffin.

Atropin should be used in all cases in which the cornea is involved and a 1 per cent. solution instilled twice a day will usually be found to keep the pupil well dilated. As a rule, atropin may be discontinued in two or three days, but not in those cases with marked corneal involvement.

Cocain should not be used as a routine, but is valuable for the first examination of the eye to relax the spasm of the lids.

Dionin in 5 per cent. solution has been tried in gas cases but discarded.

When hyperemia of the conjunctivæ exists for a long time a mild astringent collyrium may be used.

As the irritation subsides the corneal condition clears and the injection begins to disappear. Then it is very important to get these patients up and to accustom them to a greater degree of illumination.

AN INFLUENZA EPIDEMIC IN SOLDIERS.

BY SAMUEL BRADBURY, M.D.,

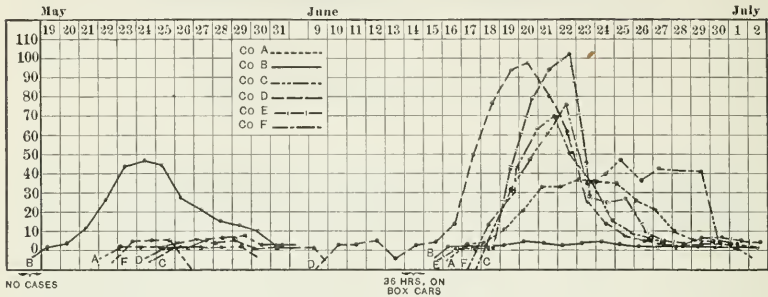
FIRST LIEUTENANT, M. R. C., UNITED STATES ARMY.

DURING the early summer of 1918 an epidemic of what was probably influenza occurred in this regiment, 11th Engineers, and for a time seriously impaired its working strength. The explosive nature of the epidemic, the comparative mildness of the disease and short duration of illness in each case, the absence of complications and yet the extraordinary manner in which the disease cut down the number of effectives are of interest. The daily incidence of new cases and the number of days each man spent in quarters were determined from the daily sick reports of the companies. Remarks on the disease itself and on the temperature associated with it are from notes and temperature charts prepared during the latter part of the epidemic.

In May and until June 13 the entire regiment was camped on a wooded hill, the tents being scattered under the trees to obtain the best concealment, but company grouping being maintained. On the latter date the regiment moved and on arrival at the new location, on June 15, camp was pitched in the regulation manner in an open field. On June 18 Company E left this camp, moving about one hundred miles, and on June 19 Company C and the Headquarters Detachment moved about ten miles distant. The remaining companies preserved their original locations and arrangements until the early part of July, when the epidemic had subsided. During all of this period the weather was very dry and at each camp dust from the roads was very heavy. It is thought that the railway journey, with the men crowded into box cars, had considerable influence in the increase of the infection in all companies after June 13.

In the whole epidemic cases occurred in two distinct groups: The first group, May 19 to June 8, included 95 cases, 65 of these being in Company B, and the second group, of 518 cases, June 9 to July 3, occurred throughout the regiment, with but 9 cases in Company B, and of these 6 were in the company officers, where the infection had not been previously. The Medical, Transportation and Headquarters Detachments each had its epidemic, but these cases have not been included in this report. One note was made in the cases in the Medical Detachment; the enlisted men here were caring for the sick, were thus freely exposed and nearly the whole detachment was taken ill during the first period.

The course of the disease in each company during each period is graphically represented in the following chart:



The disease appeared in Company B on May 19. By May 21 there were 11 men in quarters, some of them apparently quite sick. A quarantine was then established over the whole camp and between the companies. Also, the men as they reported sick were grouped into isolation tents and there kept strictly away from the well men in the company, even their food being brought to them by enlisted men of the Medical Corps. Company B developed 65 cases; the largest number admitted was 19 on May 22 and the greatest number in quarters on one day was 47 on May 24. The other cases were: 8 in Company A, 11 in C, 5 in D, 6 in F and none in Company E, a total of 95 cases, with a loss of 408 "man days." By June there was but 1 case, in Company A; in camp. Four days later 5 new cases had appeared in Company D. The following day, June 13, as the regiment had orders to move, every case in camp was sent to hospital. The move was made in the usual freight cars, 22 men to each car, and consumed thirty-six hours. On the morning of arrival, June 17, there were 7 new cases, all in Company D. On June 17 there were 36 new cases admitted, and this company epidemic reached its high mark of 98 cases in quarters on June 20. In Company F the first case was on June 17; there were 28 new cases on June 19 and on June 21 there were 70 men in quarters. Company E had 2 cases the day of its departure, June 18, and the next day 41 cases were admitted, with the greatest number in quarters, 102, on June 22. Company C left the morning of the 19; by "Taps" that night had admitted 30 men and reached the high mark of 77 on June 22. The epidemic in Company A was not so explosive in character, the greatest number in quarters at any one time being 38 and the largest number of admissions 15, both being on June 23. Cases in all companies in the second period totalled 518, with 70 in Company A, 9 in B, 115 in C, 123 in each of D and E Companies and 78 in F, with a loss of 2198 "man days." In the whole epidemic there were in the 6 companies 613 men sick, and it was found that the average time in quarters was 4.26 days per man. After discharge from quarters they were allowed to remain at some light duty

for one to three days. There were 22 men sent to hospital, including 7 cases sent on June 13 when the regiment moved. The time lost by these hospital cases and that by the men on light duty has not been included in the estimate of time lost, as neither could be accurately estimated. It is interesting to note the few cases in Company B in the second period, showing that the company was rendered immune by the earlier infection. That immunity was slight or of short duration is evident, as there were undoubted recurrent cases.

The onset of the disease was sudden, often developing in a few hours, with fever and chilliness, prostration, headache and vertigo. There was usually general muscular soreness, an irritative non-productive cough, a slightly sore throat and injected conjunctivæ, and constipation often obstinate. The headache was frontal, usually severe and often described as being in or behind the eyeballs; muscular pain was most severe in the lumbar region, but a number of men complained of severe pain in the muscles of the upper abdomen. In a few cases there were diarrhea and vomiting at the onset. Nearly every case was marked by 3 outstanding features: a thickly coated tongue, marked enlargement of the glands over the mastoid process and a red throat with slightly swollen tonsils, the tongue especially being distinctive, with a thick moist yellow coat. In many of the cases with high fever and severe headache the face was reddened and appeared slightly swollen; the neck was slightly stiff and there was a blotchy erythema over the chest and upper abdomen. A certain number of these severe cases had a patch of apparent ecchymosis in the soft tissues of each upper eyelid. Drowsiness was marked, most of the men sleeping all day, and if wakened very soon dozing off again. Epistaxis was noted in about 30 cases. Cough was nearly always present, frequent and harassing for the first two or three days, then usually disappearing altogether, but often becoming loose, with mucopurulent expectoration. Delirium was noted but once. Except for a few cases which developed severe bronchitis examination of the heart and lungs was negative; the spleen was not enlarged and reflexes were normal. In 211 cases from Companies A, B, D and F records of the temperature (by mouth) were kept. In this series the average duration of fever was 2.25 days. Some men had fever for but one or two observations; the longest duration of fever in which no complications were found was in 10 cases five days, all but 3 of which had temperatures higher than 103° F. It was not the rule, however, that high fever was of longer duration. Two of the patients with temperatures over 104° F. had but two days of fever, and of the cases with 103° F. or more 2 had fever for a day and 22 had but two days of fever. The highest temperature was 104.6° F. There were 64 cases whose temperatures reached 103° F., and of these 15 had 104° F. or more. In 16 cases the fever did not reach 100° F. The highest point in the fever curve was reached on the first day in 152 cases, on the second day

in 56 cases and on the third day in 3 cases. Defervescence occurred rapidly, *i. e.*, in twelve hours, in 113 cases and gradually in 98 cases. After fever had disappeared physical weakness was marked for two or three days and the men were not, as a rule, fit for duty in less than four days. Often backache persisted for several days after the disappearance of the fever.

Complications were quite uncommon, there being 4 cases of bronchopneumonia, 1 case of frontal sinusitis, 2 cases of discharging ears, both in men who had a chronic suppurative otitis media, and about 10 cases of severe laryngitis. There was 1 death, bronchopneumonia, occurring some days after the soldier had been sent to the hospital. A number of cases relapsed in two or three days after being allowed up. These relapses were, as a rule, more severe than the primary attack, especially in the respiratory symptoms, though the lungs were negative to physical examination. Second attacks, occurring two weeks or more after the first attack, were seen, but were uncommon.

Medication was limited to an initial purge and sodium salicylate. On a number of cases acetphenetidin was tried, but these men were not as comfortable and the muscular pain especially was not relieved. In 2 cases the sodium salicylate was held responsible for nausea and vomiting. All were given a light diet, mainly soups and toast, and an effort was made to keep every case in bed until fever had disappeared.

REVIEWS

SYPHILIS AND PUBLIC HEALTH. By EDWARD B. VEDDER, A.M., M.D., Lieutenant-Colonel, United States Army. Pp. 314. Philadelphia and New York: Lea & Febiger, 1918.

THE author of this book has compiled the important features of syphilis in its relation to the public health, both from the military and civil standpoint, in the United States.

In view of the great prevalence of the disease and its almost complete lack of sanitary control in civil communities, this book, appearing from the pen of a well-recognized military authority at a critical time in the nation's history, is particularly pertinent, and because of the completeness and conclusiveness of the statistics furnished should command the serious thought and consideration of all physicians, laymen, legislators and public health officials. The morbidity and mortality of syphilis, as attested by life insurance companies and syphilologists generally, is accorded detailed description. The book contains four chapters devoted to the prevalence of syphilis, the sources of infection and methods of transmission, personal prophylaxis and public health measures. In the appendix the technic of the Wassermann reaction is described, and the critic feels it his duty to take certain exceptions; notably to the employment of double units of complement and amboceptor, reliance exclusively upon the use of cholesterinized antigen and the employment of amboceptor "papers" instead of the properly preserved liquid. As a whole the work contains much interesting, valuable and indispensable knowledge and is destined to occupy a foremost place among the best contributions to this much neglected and timely sanitary problem.

B. A. T.

SCOPOLAMIN-MORPHIN SEMINARCOSIS DURING LABOR. By WILLIAM OSBORNE GREENWOOD, M.D. (LEEDS), B.S. (LOND.). Pp. 115. London: Oxford University Press, 1918.

THIS brochure is a monograph which is intended to show that the suffering during labor is reduced by means of the use of scopolamin-morphin seminarcosis, while the risks vanish to a negligible

quantity when reasonable care is used. The author has had quite an experience with this method of conducting labor, and in order to properly answer all the queries that have been directed to him, he deemed it best to present the available literature, together with his own personal beliefs and experiences, in this little volume.

Throughout the work the author is careful to discriminate between amnesia and analgesia, since the former state is the one desired in this work, while analgesia is unnecessary and represents, as a rule, an overdose of the narcotics. It is of interest to note that the author suggests that the birth-rate of England, which has fallen as a result of the war, might be considerably increased if the women could be assured that labor can be made practically painless by the application of this technic. The book is well written and amply fulfils the purpose for which it was intended. F. B. B.

MILITARY SURGERY. By DUNLAP PEARCE PENHALLOW, M. R. C., U. S. A.; Chief Surgeon, American Women's War Hospital. Second edition. Pp. 519; 225 illustrations. London: Henry Frowde and Hodder & Stoughton, 1918.

MANY books intended to cover the needs of the beginner in war surgery published since this war began have been new editions of works in use before the war which have been changed in varying degree to meet the new conditions. This applies particularly to the operative surgeries. Penhallow has devoted himself entirely to military surgery as it has been developed by this war, and particularly as it has developed in his own hands from a wide personal experience. The great difference between military and civil practice makes necessary attention to detail in connection with the more severe varieties of war wounds, the character of the missiles producing them, the difficulties of transportation and the severe infective and other complications which arise. In this second edition the chapter on treatment has been entirely revised and the methods brought up to date so far as possible. One chapter is devoted to a description, with many good illustrations, of the various missiles used in this war, including the various kinds of shells, shrapnel, grenades, bombs and mines. There are also numerous illustrations of wounds produced by these missiles and their fragments. The advances made in the treatment of infected wounds are given prominence, while the greatest part of the book is given up to a systematic discussion of the wounds of the various parts and tissues of the body, case reports being made use of very

frequently. Its chief virtue is in the intimate touch it affords with the actual conditions in the surgery of the present war. In this way it must be of much value to the surgeon about to enter this field.

T. T. T.

A TEXT-BOOK ON GONORRHEA AND ITS COMPLICATIONS. By GEORGES LUYS, late Assistant to the Urological Clinique, Hôpital Lariboisière, Paris. Translated and edited by ARTHUR FOERSTER, late Resident Medical Officer, London Lock Hospital. Second revised edition. Pp. 386; 201 illustrations and 3 colored plates. New York: William Wood & Co.

THIS work ranks as one of the very best if not the foremost on the subject of gonorrhœa and its complications. From a prolonged experience the author has learned the absolute efficiency of certain remedies over others that for generations have been routinely described in text-books and possessed comparatively little or no value. He therefore has avoided enumeration of these old obsolete methods and has given a full description of the modern and more accurate therapeutic measures leading to certain cure. The first edition of Luys' *Traité de la Blennorrhagie* appeared in 1912. Since then it has been translated into Spanish, Russian and English.

The book contains twelve chapters. The first is of historical interest and presents the development of our knowledge of the etiology and therapy of the disease. The following chapters deal with the gonococcus in its biological, staining, cultural and clinical aspects, referring especially to its dangers and the social and legal questions relative to gonorrhœa. A chapter is devoted to the non-gonorrhœal urethritides. The anatomy of the urethra and its appendages and the pathology of gonorrhœa are specially considered. The clinical picture of the disease, including the symptomatology, diagnosis, and treatment of the disease, is given careful, accurate and complete attention. Urethroscopy as an essential to proper diagnosis and treatment in selected cases is naturally accorded a most important and valuable chapter by one of its recognized masters. The numerous complications of the disease are fully described and a special chapter is devoted to gonorrhœa in women and children. The last two chapters, which are most important, give a full description of the treatment of acute and chronic gonorrhœa. Emphasis is bestowed upon those therapeutic measures that have withstood the test of time and if properly applied lead to certain cure.

In the group of complications the critic notes the absence of mention of gonorrhœal roseola, a rare but certain occurrence. The reviewer observes the author's chief reliance on endo-urethral cauteri-

zation with the galvanic cautery for the treatment of all papillomatous proliferations of the urethra and feels it his duty to direct attention to the superiority of electrocoagulation or fulguration for the destruction of these excrescences.

The book is well illustrated, largely with original figures, a noteworthy feature in this new edition being the omission of a number of figures showing instruments of German manufacture. Two new illustrations have been added. Other changes noted are the strong advocacy of colloidal preparations, especially colloidal silver. The translator and editor has added a few remarks on electrical treatment and vaccines and has made other revisions in the text where it was thought to be advisable. The publishers are to be commended upon the excellence of type, freedom from typographical errors and admirable character of the illustrations.

B. A. T.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE,
MARYLAND,

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF
CINCINNATI, CINCINNATI, OHIO,

AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

Experimental Meningococcus Meningitis.—AUSTRIAN (*Bull. Johns Hopkins Hosp.*, No. 330, xxix). Owing to the circumstances under which research was carried out monkeys were not available. Rabbits were used. Cultures of meningococci which were introduced into the spinal canal in the lumbosacral region produced a rapidly fatal inflammatory reaction most marked at the base of the brain. In certain instances, positive cultures were obtained from the nasal mucous membrane. In only two of ten animals did invasion of the blood stream occur. In a new series of twenty rabbits, suspension of meningococci were injected into the nasal mucous membrane. None of these animals developed meningitis. Two developed positive blood cultures. This may have been due to the direct injection into the small bloodvessel. In another series of fifteen rabbits similar suspension was injected into the ear vein. Meningococci disappeared from peripheral circulation within an hour and a quarter and none of the animals developed meningitis. Hyperemia of the choroid plexus and of the meningeal vessels was produced by preliminary irritation of the meninges produced by injection of normal rabbit serum and from thirty to fifty minutes later the animal was given an injection of standard suspension of the meningococci into the ear vein. In two animals of twenty so treated, killed one hour after injection, meningococcus was found in smears and was obtained from the spinal canal, in one, in pure culture. Three other animals developed typical fatal meningitis. From the

above the author believes it is demonstrated that meningococcal sepsis in the rabbit may lead to the development of a metastatic meningitis when there is a præexistent hyperemia of the meninges.

Peptic Ulcer, with Special Reference to Roentgen-ray Diagnosis.—**BAETJER** and **FRIEDENWALD** (*Bull. Johns Hopkins Hosp.*, No. 330, xxix). An additional series of 743 cases of peptic ulcer has been followed not only clinically but by careful roentgen-ray study. In 185 cases, the diagnosis was definitely proved by operation. In 323, clinical symptoms as well as positive roentgen rays indicated that the diagnosis was undoubtedly correct; 235 cases lacked some important signs, although in a large number the roentgen-ray findings were definite. From this study the authors conclude: (1) The roentgen rays offer most valuable assistance to the diagnosis of peptic ulcer, and although this method is not yet sufficiently well developed to be relied upon alone without entering into the clinical aspects of the disease, it is of the greatest diagnostic help in obscure cases. Positive roentgen-ray findings are noted in about 84 per cent. of cases of peptic ulcers and in 79 per cent. of cases operated upon. (2) In duodenal ulcer there is excessive hypermotility of the stomach with rapid evacuation of the contents, so that the greater portion is extruded within the first half-hour; there is hypermotility of the duodenum with formation, usually, of a deformity which remains fixed in all of the examinations. (3) The diagnosis of gastric ulcer is dependent upon two conditions, namely, the functioning of the stomach and the finding of the filling defect. It is only when the filling defect is situated along the anterior surface of the stomach and along the anterior surface of the lesser and greater curvatures that it can be demonstrated. On the other hand it matters not what the situation of the ulcer is, the functions of the stomach are materially affected. We have in this condition an excessive irritation from the ulcer, with consequent hypermotility and a spastic condition of the pylorus, so that for the time being there is practically no expulsion of bismuth. It is only when the spasticity relaxes that a portion of the bismuth is expelled. In gastric ulcer, wherever its situation, we can always look for a certain amount of retention of contents. There is always a more or less marked hour-glass formation. According to our observations the functional signs are often as important as the presence of the filling defect in arriving at definite conclusions, inasmuch as in 8 per cent. of our cases, although there were no defects found, the functional changes pointed definitely to ulcer. (4) The greatest difficulties arise in the diagnosis of complicated cases; that is, when adhesions are present. These so frequently mask the usual findings that it is often impossible to determine whether there is really an ulcer of the stomach at hand or a lesion of some other organ. When the ulcer is situated at or near the pylorus, signs of partial obstruction frequently aid in establishing the diagnosis. (5) The roentgen rays afford an almost absolute means of differentiating between gastric and duodenal ulcer. (6) By means of the roentgen-ray examination we generally rule out the presence of ulcer. (7) We can approximately determine the degree of healing as well as recurrence of an ulcer which cannot be as certainly determined in any other way. (8) One can

obtain sufficient evidence as to the extent and induration of the ulcer and degree of obstruction to guide us, in a measure, as to the necessity of surgical intervention.

Clinical Study of 400 Patients with Bronchial Asthma.—WALKER (*Boston Med. and Surg. Jour.*, August 29, 1918). All patients were tested by the skin or cutaneous method for sensitization to the proteins of animal hair or dandruff, food, bacteria and pollens; 48 per cent. gave a positive skin test, the criterion for a positive test being an urticarial wheal measuring at least 0.5 cm.; "75 per cent. of the patients who began to have asthma during infancy (under the age of two) were sensitive; between the ages of two and fifteen, 66 per cent. were positive; between the ages of fifteen and thirty-five, 52 per cent. were positive; between the ages of thirty-five and fifty, 23 per cent. were sensitive; and none were sensitive when the age of onset was after fifty." Walker shows that sensitization to the protein in animal hair (horse, dog, cat, wool) was most marked under ten years of age (45 out of 75 sensitive cases) and that succeeding ages show a gradual decrease in number thus sensitive. Sensitization to food proteins apparently is much more common in infants. Of all food cases one-half were sensitive to cereals, wheat being the chief offender; next to wheat ranks the egg, while fish, potato and casein are close thirds. In the case of pollen proteins, timothy and ragweed hold chief place among the early and late pollens, respectively, while in the author's findings sensitization to rose, red top, daisy and golden rod was infrequent. All ages up to forty showed about the same frequency of sensitization to bacterial proteins, more being sensitive to *Staphylococcus pyogenes aureus*. As to treatment the author says: "If a patient is sensitive to food proteins, such food should be omitted from the patient's diet for at least a month. In this series of cases nearly all such patients have been relieved of asthma. Attempts to desensitize the patient against offending food protein by the subcutaneous injection of or by feeding gradually increasing amounts of the protein have failed. We have reasons for believing that total abstinence from the offending protein for a long interval automatically desensitizes the patient for that protein. Patients who are sensitive to bacterial proteins may be successfully desensitized against such by treatment with vaccines of those organisms. Patients who are sensitive to pollen proteins should be treated in anticipation of the season."

Influence of Menstruation on Acidosis in Diabetes Mellitus.—HARROP and MOSENTHAL (*Bull. Johns Hopkins Hosp.*, July, 1918, 161). The authors give detailed study of a very severe case of diabetes mellitus in a colored girl, aged eighteen years, whose tolerance for carbohydrates was unaffected by starvation. During her stay in hospital she menstruated once. At the onset she complained of abdominal pain, refused food, developed hyperpnea and drowsiness, and there was involuntary twitching of the facial muscles. Laboratory data showed increase in acidosis. With cessation of flow all symptoms of coma disappeared. During the next period while at home the patient went into a state of coma and died.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Further Observations on the Results of Blood Transfusion in War Surgery.—ROBERTSON and WATSON (*Ann. Surg.*, 1918, lxxvii, 1), in a previous paper, gave the results of blood transfusion in a few cases of secondary hemorrhage, with a description of the Lindeman syringe-cannula method. Since that time opportunity has arisen of extending its application to cases of severe primary hemorrhage accompanied by shock. The results of these cases are presented in this paper. They have shown: (1) That certain cases heretofore considered as inoperable and others exceedingly bad surgical risks often may be revived to a degree which not only permits of radical operative measures but ensures a good prospect of ultimate recovery. (2) In other cases in which the postoperative condition is one of progressively increasing shock, due to the initial loss of blood and to the severity of the operative measures required, blood transfusion is a permanent resuscitative measure of extreme value; the largest factor in the causation of the shocked condition as seen in patients admitted to a casualty clearing station appears to be the loss of blood, except in the case of visceral injury. In 2 cases hemolysis hastened the death of the patient—in one of these the citrate method was used. The possibility of hemolysis certainly is present, but the danger of its occurrence is slight in comparison with the danger of operating on a shocked and exsanguinated patient. The results in this series of 36 patients of severe primary hemorrhage may be classified as: life-saving, 22; immediately beneficial but died from infection or operation, 9; no benefit, 3; harmful, 2; total, 36. Although the mortality in this series of cases is comparatively high it must be remembered that all the patients were in a desperate condition, and with perhaps one possible exception could not have been expected to survive if the procedure had been withheld.

The Use of Dichloramine-T in Wounds.—LEE and FURNESS (*Ann. Surg.*, 1918, lxxvii, 14) say that from comparative studies on large numbers of cases between the results obtained from the Carrel technic and Dakin solution and the dichloramine-T with a simpler technic they have been able to obtain as good results from the latter as they ever obtained with the former. In addition they found: (1) That skin irritation will not occur if the wounds are not covered with thick occlusive dressings; this means the use of the smallest possible amount of gauze dressings and bandage. (2) The small amount of exudates from wounds treated with dichloramine-T makes it practical to use these thin dressings, and in their dispensary at the Pennsylvania Hospital there has been a saving of 75 per cent. of the gauze and bandages formerly used. Further, a

still greater saving in dressing material and time results from the decrease in the number of the dressings required for each wound during the period of healing. Rarely is it necessary to dress a wound, even during the first few days, more frequently than once in every twenty-four hours, and after that, intervals of forty-eight and seventy-two hours are usual. (3) Dichloramine, unlike the aqueous hypochlorite solution, has no effect upon the knots of catgut ligatures and no disintegrating effect upon the catgut itself. The occurrence of secondary hemorrhages in wounds treated by the Carrel method was not uncommon in their experience in the American Ambulance. Captain Sweet reports that in his 1200 cases of major infected military wounds treated with dichloramine-T there was not one secondary hemorrhage. (4) Two great stress cannot be laid on the value of dichloramine as a deodorant dressing. The absence of the usual disagreeable odors in their wards containing fecal fistulae is a general observation. During the last two months it has been used routinely in the wards of the Oncologic Hospital in Philadelphia. Where formerly these putrid, sloughing, malignant tissues were irrigated every two hours with all kinds of solutions, with indifferent success in the control of infection and with a persistence of the offensive odor, now they are packed lightly every six hours with gauze saturated with a 5 per cent. solution of dichloramine-T. Not only has the odor disappeared entirely but the wound infections have been controlled. At the primary operation all foci of infection and of devitalized tissue must be removed when possible by surgical procedures.

Clinical Study of Blood-pressure and Hemoglobin in Postoperative Shock, Hemorrhage and Cardiac Dilatation.—POLAK and HEFFTER (*Surg., Gynec. and Obst.*, 1918, xxvi, 312) say there is a constant rise of 5 to 15 points in the hemoglobin readings following anesthesia with ether when such anesthesia occupies more than thirty minutes. Consequently, allowance must be made for this rise in using hemoglobin estimations as a diagnostic sign in internal bleeding. The erythrocyte count is also increased, but its variation from the preoperative is so slight that it does not warrant any conclusions. In the majority of cases there is a moderate fall in both the systolic and diastolic blood-pressure following ether anesthesia. The blood-pressure returns to the normal, that is, to the preoperative reading in twelve to forty-eight hours. The inhalation of oxygen after the withdrawal of the ether vapor diminishes this fall in blood-pressure, but is only transient in its effect. In cases of shock, especially when there has been much blood lost during the operation, the fall in blood-pressure is greater than after long operation without blood loss, dropping from 10 to 5 mm. The pulse-pressure is a better index of hemorrhage or cardiac failure than the systolic pressure. There is a constant rise in the leukocyte count in hemorrhage while the leukocytes fall in shock.

Provocative Wassermann Test in the Clinical Diagnosis of Syphilis.—STOKES and O'LEARY (*American Journal of Syphilis*, 1917, i, 629) says that the so-called provocative Wassermann test is based upon an observation made by Gennerich in 1910 and confirmed by Milan, to

the effect that a syphilitic serum weakly positive or even negative before can be rendered strongly positive following an injection of salvarsan. Gennerich conceived the reaction to be a phase of the Herxheimer reaction and ascribed to it considerable value in the detection of latent syphilis, especially in cases in which treatment had been given followed by a rest period. From a study of 103 cases in which an injection of salvarsan was given to provoke a positive Wassermann after a negative test, presumptive, but not conclusive evidence of a provocative effect was obtained. A knowledge of the tendencies and limitations of the Wassermann technic employed should form a part of any study of the clinical value and interpretation of the provocative Wassermann test. Such a study on a series of repeated Wassermann tests in the Mayo Clinic seemed to indicate that the tendency of the technic was conservative and against the conversion of negative into positive reaction without the administration of salvarsan. It seems probable that both individual technical variations and variations in the reagents are a factor in the results in addition to the provocative effect. Positive provocative effects were obtained in 18.4 per cent. of 103 cases. The provocative test was of value in recognizing as insufficiently treated 2 out of 6 cases (33.3 per cent.) in which it was applied to determine whether a cure had been attained. A strictly controlled and completely worked-out provocative procedure involves an amount of labor which makes it clinically inapplicable, and it seems probable that this same obstacle will keep it in the field of presumptive rather than conclusively demonstrated clinical phenomena. The provocative test in their series seemed to be of service in active deep-seated visceral, osseous and central nervous system syphilis, where it was most needed, fairly efficient (40 per cent.) in latent syphilis and most often positive in late cutaneous and mucous membrane manifestations where the diagnosis can often be made morphologically. Their results do not suggest that the provocative is entirely a Herxheimer reaction phenomenon, since local and symptomatic Herxheimer reactions occurred in our series in cases in which no provocative effect could be recognized as well as in cases showing a provocative effect. It is possible, however, that the use of several very sensitive antigens might demonstrate an effect not detected in routine procedures. At its best the test yields a rather small return for the amount of trouble, and if overelaborate is subject to the same risk of error as the oversensitive Wassermann test. The percentage of cases whose syphilis was suspected from clinical examination ran parallel to the percentage shown to be syphilitic by therapeutic test and far in advance of the number shown to be syphilitic by the provocative test. Positive therapeutic effects were obtained in 63.1 per cent. of 38 cases and in 65.2 per cent. of 23 cases in which the provocative test had failed to establish the presence of syphilis. The provocative Wassermann would seem to be of little value in the absence of clinical evidence of the disease, and to be inferior both to clinical judgment and the therapeutic test in the recognition of obscure cases.

Acridiflavine and Proflavine.—CARSLAW and TEMPLETON (*Lancet*, May 24, 1918, p. 634) say that both substances have been extensively observed, clinically, histologically and bacteriologically, and it is now

permissible to formulate several conclusions which apply to the action of both: (1) Action on bacteria in infected wounds: The application of flavine to infected wounds does not render them bacteriologically sterile. Flavine is clearly antiseptic, not disinfectant, in action. The diminution in the numbers of the organisms might suggest a bactericidal action, but their persistence and viability favor the view that the absence of inflammation and suppuration may be due to neutralization of the toxins. Bacteriological investigation is of little value in judging of the progress of the wounds. (2) Action on tissues: There is a complete absence of evidence of damage to the tissues when these salts are used in solutions not stronger than 1 to 1000. There is no necrosis of any of the exposed tissues. The writers disagree absolutely, with the opinion expressed by Fleming regarding the action of flavine on leukocytes. Whatever be its effect on these cells *in vitro* their activity in wounds was unimpaired after many days' exposure in this antiseptic. The reparative changes are undoubtedly delayed to a certain extent. (3) Value in treatment of infected wounds: These salts are of undoubted value in controlling and preventing the spread of sepsis, as is shown by the rapid improvement in local and general conditions. This object having been obtained there is advantage in continuing their use, as a condition is reached in which reparative changes are slow, although not by any means absent. Following on the substitution, after a few days, of a more stimulating antiseptic, *e. g.*, eusol, a "clean" wound is obtained sooner than by any other form of treatment known to the writers. Owing to the limitation of sepsis and the consequent small amount of sloughing there is much less liability to secondary hemorrhage. There is no evidence of any general toxic effect. (4) Essential points in treatment: (a) Necessity for adequate preliminary surgical measures; (b) necessity for continuous supply of the antiseptic to all parts of the wound; (c) no necessity for frequent changes of the dressings; (d) the formation of the fibrinous membrane is a useful clinical guide, indicating when a more stimulating antiseptic ought to be substituted.

Osseous Cysts and So-called Giant-celled Sarcomata.—PLATOU (*Ann. Surg.*, 1918, lxxvii, 312), of Christiania, Norway, on the basis of a clinical and histological study of this subject, concludes that *ostitis fibrosa* with formation of tumor is not very rare. It occurs most often in young individuals, but may also be found in persons of fifty to sixty years. Trauma appears in many cases to be an etiological factor, although we are unable to explain how it can cause the disease or influence its genesis. The course of the disease is chronic, with comparatively slight symptoms, rheumatic pains and a slow swelling of the affected bone. The general health is good. Spontaneous fracture or bending of the bones may occur. The roentgen photograph is often typical, but sometimes it is impossible to decide whether the diagnosis might not with equal correctness be given to sarcoma. The treatment is exclusively surgical, all diseased tissue must be carefully removed, albeit with an obligation to be as conservative as possible. When the bone is opened the cavity is found to be more or less filled with a brownish-red or sometimes yellowish, crumbling tumor tissue.

The borderline is, as a rule, sharply drawn, although the same tissue may be found outside the periosteum. Under the microscope the destruction of the bone is seen to take place in a connective tissue with a few cells, *i. e.*, fibrous marrow. Formation of new bone is also seen. The tumor-like mass is built up partly by very polymorphous cells, with numerous and uncommonly large giant cells, partly from a fibrous tissue with few cells. Mucous tissue with softening and formation of cysts also occurs. It is sometimes difficult to decide that the diagnosis is not sarcoma. The disease is benign even when the periosteum is perforated.

Regeneration of Bone.—BERG and THALIMER (*Ann. Surg.*, 1918, lxxvii, 331), from an experimental study and a review of the literature, say that periosteum devoid of adherent bone cells when transplanted into foreign tissues produces bone. Endosteum and osteoblasts lining Haversian canals in bone transplants produce bone very actively. The cambium layer when adherent to transplanted cortex produces bone. Some bone cells in the transplants are able to persist for almost a year, but most of the bone is absorbed. Fully developed adult bone cells, although they may remain alive for a considerable period, do not reproduce themselves and form bone. Very young lacunar cells (frequently erroneously called bone cells) can reproduce themselves and form new bone. Transplanted bone is absorbed not only by osteoclasts but also by a direct action (biochemical?) of growing, young bone, and the transplanted bone is replaced either by a creeping forward of the new bone or a gradual extension or expansion of the new bone into the transplant. Marrow spaces and hematopoietic marrow are formed in the bone which develops from transplanted periosteum. The source of these hematopoietic cells was not determined. Bone, when it grows into cartilage, does so in the same manner characteristic of the normal embryonic development of enchondronal bone, including also epiphyseal line formation.

Through-and-through Ramrod Wound of Head.—STUART (*British Med. Jour.*, April 27, 1918, p. 481) reports the case of a girl, aged eight years, brought to him with the ramrod of a gun fixed firmly in her head. It appears that a gun had been left on a shelf, loaded with the charge of gunpowder only and the ramrod left in it. The child in pulling something off the shelf had caused the gun to fall forward, when it went off. The ramrod had entered the cranium one inch above the top of the forehead, half an inch to the left of the middle line, and was protruding for some four or five inches from a point half an inch to the right of the same line and two and a half inches above the occiput. On admission the child was conscious but the pulse was scarcely perceptible. There was no bruising of the skin nor any hemorrhage, and the ramrod was so firmly fixed in the skull that the point had to be sharply tapped with a mallet in order to loosen it sufficiently to allow of its removal. For this the child was given chloroform and the head shaved and the protruding end of the ramrod was painted with iodine before putting it back through the skull. Very slight hemorrhage at the point of exit followed the withdrawal. For

the first two days the patient vomited when any food was given her by mouth, and for the first day the pulse was very low (48) and intermittent. By morning it was regular and of good volume. The temperature was 100.8° on the first night, but by morning of the second day both temperature and pulse were normal. During the next few days the pulse was occasionally irregular and she complained a good deal of headache, but otherwise she made an uneventful recovery. The little punctured wounds healed in two or three days by first intention, and she was dismissed in perfect health in three weeks, having been kept in hospital long enough to make sure that no cerebral symptoms would develop later.

War Surgery.—VIANNAY (*Lyon Chirurgical*, 1918, xiv, 921) says that operation should be done as soon as possible after the injury is received, with the removal of all foreign bodies from the joint, thoracic cavity or cranial cavity, except only in those cases in which the foreign body is buried too deeply in the brain substance. One should practise excision of the whole track of the projectile if only soft tissues are touched, but if there is a fracture, fragments should be removed subperiosteally and the marrow cavity opened to be sure that no septic body remains. Technical details are given in connection with the treatment of each region, emphasis being laid particularly on articular injuries. Arthrotoomy is recommended, to be followed by primary suture in those cases in which the projectile only opens the synovial cavity without injury to the bone or with limited fracture. Primitive subperiosteal resection is recommended in every case with epiphyseal or diaphyso-epiphyseal fracture. The author further discusses the opportunity of primitive suture and brings personal statistics of 222 cases with 96 per cent. success. Primitive suture is always advisable when there is not a too great affluence of wounded and when the surgeon can keep his patients for a sufficiently long time. If conditions are not propitious for primitive suture the author prefers a secondary suture during the first week after operation or even later, sterilization of the wound being obtained. The presence of streptococci constitutes a contra-indication. The author presents a splendid series of sutures of fractures, *i. e.*, suture of the soft parts in fractures, transforming by this method open fractures into closed fractures. This method may be employed in fractures by the contact of the projectile without penetration into the bone, or even if thorough cleansing of the focus is ensured by minute intervention.

Ambrine and a Gutta-Percha-Paraffin Substitute.—ROBERT (*Lyon Chirurgical*, 1917, xiv, 1048,) states his experience with ambrine and gives the formula (paraffin at a temperature of 48° to 49° C., 100 gr., and natural gutta-pecha, 3 gr.) of a substitute which has the same physical chemical and therapeutic properties as ambrine, the composition of which has not yet been published. The method of application and the clinical results are identical with the two preparations. The dressings with both offer the inconvenience of favoring stagnation of the pus. The author, therefore, reserves them both for large, dry wounds. If a wound is still discharging, he prefers dressing

it with loosely woven gauze, saturated with the paraffin mixture instead of impermeable layers of sheet wadding. The therapeutic action of both preparations is due to impermeability to water and wound secretions, and thus in absence of contact with the elements of the wound. It protects the wound without sticking to it and thus renders dressings painless.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

Etiology of Epidemic Poliomyelitis.—The results of a series of observations by TSEN (*Jour. Exp. Med.*, 1918, xxviii, 270) may be summarized as follows: The animals used in these experiments were monkeys and rabbits. Streptococci were isolated from the central nervous system of monkeys dead of poliomyelitis, from the central nervous systems of monkeys dead of other causes and from the brains of normal rabbits. The streptococci isolated from poliomyelitic monkeys did not differ from those isolated from monkeys and rabbits dead from other causes and no etiology was established between the streptococci and poliomyelitis. The writer several times isolated an organism similar to the globoid bodies culturally, morphologically and in staining reaction, but was not able to carry it along for more than three generations. The pathogenicity of these organisms has not therefore been tested on monkeys. Typical lesions of poliomyelitis were not produced in rabbits by the injection of either the poliomyelitic virus or the streptococci.

The Pharmacology of the Oil of Chenopodium.—SALANT'S (*Jour. Am. Med. Assn.*, 1917, lxix, 2016) experiments on animals (rabbits, cats, etc.) indicate that oil of chenopodium, even in very small quantities, may prove very toxic. He notes that sensitiveness to the oil persists for from five to nine days and warns that the repetition of a non-effective dose within this period may cause serious symptoms or death. The toxicity of oil of chenopodium varies largely with the nutritional condition of the animal. Fasting or poorly nourished animals succumbed to much smaller doses than did those that had been receiving a diet rich in carbohydrates for several days before the oil was given or when the administration of the oil of chenopodium was preceded by a sufficient quantity of fatty oil (olive, cocoanut or castor oils). As regards the therapeutic use, Salant concludes that oil of chenopodium should be handled with caution when used for internal medication, as it has a tendency to affect the central nervous system, the heart, respiration, the digestive organs and the kidneys. In renal or cardiac disorders the oil should be given in small doses only, while in advanced cases of chronic nephritis or heart disease its use would

seem to be altogether contra-indicated. As the liver undoubtedly plays an important part in detoxifying oil of chenopodium while changes in the gastric and intestinal mucosa may accelerate its absorption into the circulation it may prove more toxic in hepatic and gastro-intestinal diseases. A diet containing a liberal amount of fats and carbohydrates, fed at least for several days before the treatment is instituted, may render the drug much safer. The routine administration of large doses of castor oil before and soon after the oil of chenopodium may prove to be of prophylactic value. In the treatment of poisoning, Salant recommends gastric lavage, since absorption of the oil from the stomach is slow; absorption from the duodenum, however, is rapid, hence lavage must not be too long delayed. No chemical antidote to oil of chenopodium has been found; the treatment therefore must be symptomatic. Experiments on the isolated heart show that digitalis and epinephrin are excellent antagonists. Caffein, on the contrary, appeared to increase the toxic action of the oil.

Study of Acute Mercuric Chloride Intoxication in the Dog, with Special Reference to the Kidney Injury.—Fifty-six dogs were employed in the series of experiments reported by MACNIDER (*Jour. Exp. Med.*, 1918, xxvii; *Jour. Pharm.*, 1918, xi, Proc.). Fifteen milligrams per kilo of a 1 per cent. solution was given by stomach tube. For three days prior to the administration of the drug observations were made on the hydrogen-ion concentration and alkali reserve of the blood, blood-urea determinations were made, the twenty-four-hour output of urine was recorded, the phenolsulphonephthalein test for kidney function and quantitative estimations of albumin were made. MacNider found marked variation in the severity of the symptoms of poisoning and in the final outcome of the experiments. He classifies the animals into four groups: Group I: The animals developed an intense gastro-enteritis and all died within forty-eight hours in a state of collapse induced through the corrosive action of the mercury on stomach and intestine. The formation of urine was greatly reduced; the elimination of phenolsulphonephthalein was not reduced proportionately to the inability of the kidney to form urine. The acid-base equilibrium was only slightly affected. The reserve alkali showed an early depletion. Group II: The animals showed a fairly severe gastro-enteritis which improved during the first few days. All the animals of this group died within seven days, some in convulsions and others in air hunger. The urine output was greatly decreased or entirely suppressed. The output of phenolsulphonephthalein showed a marked and rapid reduction, a retention of blood-urea being associated with decreased elimination of the dye. The alkali reserve of the blood was greatly decreased. The kidneys showed an acute swelling and necrosis of the convoluted tubule epithelium. Group III: The third group showed a moderately severe gastro-enteritis and developed a mild grade of acid intoxication, but succeeded in reëstablishing their normal acid-base equilibrium. All the animals of this group recovered so far as the acute intoxication was concerned. Group IV showed a type of intoxication resembling the third group. They all recovered from the gastro-enteritis. Following a period during which there was an attempt to return to normal, as

indicated by an increase in the alkali reserve of the blood and by an increased output of phenolsulphonephthalein and urine, the members of this group developed an acid intoxication and, like Group II, became anuric. The animals in all groups dying from delayed intoxication caused by mercury showed a severe type of kidney injury characterized by an acute swelling and necrosis of the renal epithelium. All these animals either gradually or acutely developed a severe type of acid intoxication. There was a definite association between the development of an acid intoxication and the delayed kidney injury, and, furthermore, the animals which showed the greatest swelling and necrosis of the renal epithelium also showed the severest type of intoxication.

Restorative Effect of Salts of Magnesium and Calcium after Lethal Doses of Sodium Oxalate.—In this series of experiments GATES (*Jour. Exp. Med.*, 1918, xxviii, 305) found that sodium oxalate injected intramuscularly into rabbits in doses of from 0.18 to 0.2 gm. invariably caused death after symptoms of excitation and tonic and clonic convulsions. If, however, small doses of magnesium sulphate (0.4 gm.) were injected intramuscularly immediately after the oxalate the development of convulsions was prevented and the mortality reduced by 80 per cent. Only small doses could be given, as previous experiments had shown that doses of magnesium sulphate and sodium oxalate, which alone produced only minor symptoms, when combined killed by respiratory paralysis 75 per cent. of the animals. Those rabbits which survived the combined dosage exhibited a depression apparently due to a specific inhibition of the nervous system, characterized by deep narcosis, anesthesia and loss of superficial reflexes. The effect of larger doses of oxalate with subminimal doses of magnesium was a kind of intoxication marked by progressive weakness ending in death. Calcium aroused these animals temporarily but had no effect on the fatal outcome. In another series of experiments the antagonistic effect of calcium on oxalate poisoning was noted. When 10 c.c. of a M/8 solution of calcium chloride was injected intravenously within one minute of the administration of the lethal dose of oxalate all the animals survived. The curative effect of calcium upon oxalate poisoning is probably due to a simple chemical process; oxalates precipitate calcium salts in the animal body, thus reducing the calcium content of the body below the amount indispensable to maintain life. The addition of calcium chloride in amounts sufficient to restore the calcium content of the body to the necessary level causes removal of the oxalate symptoms and the recovery of the animal. Gates concludes that the favorable antagonistic action of magnesium against fatal doses of oxalate is merely symptomatic in nature while the synergistic action of subminimal doses of magnesium and oxalate may be considered as specific, the seeming contradiction being explained on the assumption that "oxalates, especially in larger doses, aside from the calcium-precipitating property, exert by means of a yet unknown factor a further toxic effect which favors the development of excitation and convulsions, which in turn lead to exhaustion and death." The precipitating action of the oxalate by decreasing the calcium content increase the effectiveness of the inhibitory action of the subminimal doses of magnesium.

Influenza Epidemic in a Camp.—AVERILL, YOUNG and GRIFFITHS (*British Med. Jour.*, August 3, 1918) base their findings on 1439 cases which developed between June 21 and July 10. Most of the cases were of characteristic type, admitted to hospital with a temperature ranging from 101° to 104° , complaining of headache, lumbar backache, general muscular pains and sore throat. The majority stated that they had been suddenly taken ill. The patients looked ill, but apart from fever and some congestion of the pharynx, and in a few cases slight bronchitis, presented no other symptoms. The illness ran a short course, the average duration of the stay in hospital being five days. Usually within twenty-four to forty-eight hours after admission the temperature fell by crisis or hovered between 99° and 100° for a few days. During the period of elevation of temperature the patients slept most of the time and did not care to be disturbed. As soon as the temperature fell they sat up in bed looking and feeling well. Complications were few. Sixteen developed more or less typical lobar pneumonia; of these seven died. Bacteriological examination of smears and growth of the sputum showed two organisms which were identical with Pfeiffer's bacillus and the pneumococcus. Nine cases with marked symptoms were chosen for blood cultures; all were sterile. Of the various preventive therapeutic measures the only one which seemed to warrant further trial is spraying the nose and throat with acro-flavine solution (1 to 1000).

Clinical Report of Non-specific Protein Therapy in the Treatment of Arthritis.—SNYDER (*Arch. Int. Med.*, 1918, xxii, 224) treated 110 cases of arthritis by injecting stock typhoid vaccine intravenously. He found that this treatment was more efficacious than the usual drug treatment, often affording relief when the salicylates failed completely. The acute, subacute and chronic cases were all benefited; the first group showed the most striking effect. In some cases there was a tendency to recurrence. The symptoms, however, were milder in type and usually yielded to intensive treatment. The percentage of recurrences was no larger than that usually following drug treatment. Snyder could find no evidence that the intravenous injection of foreign protein had any injurious effect on the kidney or any other organ, and believes that with proper precautions this mode of treatment is not only free from danger but is the most efficacious available.

Report on the "Influenza" Epidemic of 1918.—GOTCH and WHITTINGHAM (*British Med. Jour.*, July 27, 1918) base their report on the first 50 cases which occurred among the members of the Royal Air Force stationed at Hampstead. The specific cause of the disease appears to be a Gram-negative micrococcus resembling in many respects the *Micrococcus catarrhalis*. Pfeiffer's bacillus was cultured in only 8 per cent. of the cases, but direct smears showed influenza-like bacilli in 62 per cent. of the cases. The authors suggest that the disease may be due to the simultaneous presence of both these organisms—symbiosis. The incubation period is short, one or two days. The onset is strikingly sudden; the patient may go to bed apparently well and wake up complaining of headache, malaise, etc., or he may be at work when he

suddenly feels giddy and in a few seconds falls to the ground in a state of collapse. The commonest initial symptoms are chilliness and malaise, which becomes quickly worse so long as the patient is up and about. Other important symptoms are general body pains, headache, tightness and soreness in the throat and nose and a slight cough. The second day finds the patient much worse. Photophobia is extreme, the patient is somnolent and the appetite is lost. The bowels are usually constipated. On the third day the patient usually feels much better, though the physical signs are more marked and the cough is troublesome. Backache (lumbar) may be very severe. The fifth day usually marks the beginning of convalescence, the patient feeling quite well but very weak. Convalescence is slow; the majority of patients do not recover their strength for a week or ten days after getting up. The physical signs are most characteristic on the second or third day. The patient appears toxic; his tongue is heavily coated and all the mucous membranes of the head are injected—there are signs of inflammation of the conjunctivæ, gums, tongue and nasopharynx. The temperature rises rapidly and is usually highest on the second or third day, and may last three or five days. Defervescence is always by lysis. By the fifth day the temperature is normal or subnormal in about two-thirds of the cases. The pulse is slow (76 to 110) even when the temperature is continuously high. Slight bronchitis is sometimes present. Pneumonia developed in four patients. The urine is scanty and highly colored; albumin was present in 90 per cent. of all the cases. In the five-day fever type of the disease hyaline and granular casts were present in 85 per cent. of the cases but only in 36 per cent. of the three-day fever type. The casts usually disappeared by the fifth or sixth day and the albumin by the eighth or ninth. The authors believe that this albuminuria is a part of the disease and is not simply an accompaniment of the fever. Blood cultures were sterile. The treatment consists of rest in bed on a milk diet. Fluids should be forced. Aspirin appears to be almost specific, 10 grains being given three times a day until temperature is normal. The bowels must be kept open. No local treatment of mouth or throat is necessary. During convalescence the diet should be light, and meats, soups, coffee and condiments avoided in view of the slight nephritis. Avoidance of bodily and mental exertion must be insisted upon until the albumin has disappeared from the urine.

Nitritoid Crises after Arsphenamin Injections.—In a series of 300 consecutive arsphenamin injections BERMAN (*Arch. Int. Med.*, 1918, xxii, 217) reports that there were eleven individuals who suffered from nitritoid crises even though they were treated with properly prepared alkalized arsphenamin injected with a technique *lege artis*. The problem which the author set himself to solve was the solution of the mechanism of these reactions. Since saline solution prepared as the arsphenamin solution was prepared failed to elicit the symptoms it was evident that foreign protein (moulds, bacteria) in the water could not account for the reactions. Schamberg's hypothetical "substance x" could not explain the crises, for the same arsphenamin was used in all the patients. Sensitization by the previous injection did not explain the anaphylactoid reaction, for in only four patients did

the crises occur on three successive occasions and in one on four. The key to the problem seemed to be found when the serum of reacting and non-reacting patients was tested with properly alkalized arsphenamin. When arsphenamin was brought into contact with the serum of non-reacting patients no precipitate or at most a faint opalescence appeared. The sera from the eleven reacting patients, however, gave a heavy whitish-yellow precipitate. Thus by testing previously the serum and the solution one could say whether or not a reaction would follow the injection. In those in whom a precipitate was produced a prophylactic dose of epinephrin seemed to prevent the onset of the nitritoid crisis. After its appearance, also, the same drug hypodermically shortened the duration of the alarming symptoms. Having determined that the nitritoid crisis occurring with sufficiently alkaline arsphenamin in certain persons was due to intravascular precipitation, the next question that arose was, Why should the precipitate be formed only in the blood of these patients and not in that of the majority who received the same amount of drug in the same physical state? Fleig had shown that most of the precipitate produced when acid arsphenamin was added to serum consisted of protein. No determinations of the content of the blood in protein in these cases has ever been made. Blood from two patients analyzed by the nephelometric method of Kober and Graves showed that there was an increased protein content, essentially an increased globulin content. The hypothesis is therefore put forward, tentatively, in view of the small number of studied cases, that this may be the solution of the problem; that is, that the increased protein content of the blood in certain syphilitics may favor precipitation *in vivo* even of properly alkalized arsphenamin.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Method of Determining the Dilatation of the External Os during Labor by External Examination.—WELZ (*Am. Jour. Obst.*, February, 1917) describes Unterberger's method for detecting dilatation of the external os uteri as practised in Winter's Clinic at Königsburg. This depends upon the fact that as soon as labor commences the contraction ring of the uterus is formed a little above the internal os. It is at the level of a large coronary vein, where the serous coat of the uterus is firmly adherent to the underlying muscle. It exists only during labor and can be felt only during labor pains in normal cases. Whether this band actually contracts or merely indicates the lower circle of contracting muscle is a question. The lower segment is dis-

tinctly thinner than the upper segment from its distention during the first stage of labor. As labor proceeds the presenting part is forced through the contracting ring of the lower segment into the vagina. As the mechanism of labor develops the contraction ring gradually rises out of the pelvis to a point about midway between the symphysis pubis and the umbilicus when dilatation is complete. The rise is in proportion to the degree of dilatation in the cervix and may be taken as an index of the degree of dilatation of the external os. When this ring cannot be felt externally above the symphysis the external os has reached dilatation corresponding in size to a silver dollar. When the diameter of the external os is 4 cm. or above the ring can be recognized two fingers-breadth above the symphysis. As dilatation proceeds the ring rises, so that when the os is about 8 cm. in diameter the ring is three fingers-breadth above the symphysis. The ring runs transversely across the uterus and is four fingers-breadth above the symphysis, with complete dilatation of the external os. The ring becomes apparent only during uterine contractions except in cases of threatened rupture of the uterus, when it may be recognized between the pains. Unterberger practised this method in 300 cases and corroborated it by internal examinations. A correct diagnosis was made externally in 95 per cent., and the 15 failures out of 300 cases were due largely to a partially distended urinary bladder. In 3 cases only, or 1 per cent., the height of the ring did not correspond to the degree of dilatation in the external os. This condition was considered abnormal, for in 1 of these patients it was necessary to incise the cervix in order to deliver. The writer is using this method, and in order to succeed with it, patience is necessary to acquire proficiency in palpation. The urinary bladder must be empty and a very fat abdomen and extremely rigid abdominal wall may defeat the purpose of the examination. The greater the degree of relaxation and the thinness of the patient the easier it is to apply this method of diagnosis. Flexing the knees has a slight influence in relaxing the abdominal wall. When conditions are favorable the lower segment can be recognized as a smoothly divided wall of tissue when dilatation is about complete, and at its upper border is the contraction ring. To feel these the finger tips should be placed lightly on the lower abdomen just above the symphysis, moving them up and down until a furrow is felt extending transversely. The writer finds that this sign is plainer in primiparæ in whom the resistance of the lower segment is great. In multiparæ repeated parturition so diminishes the resistance that the sign may be of little or no value.

Rectal and Vaginal Examination in Labor.—MOORE (*Am. Jour. Obst.*, February, 1917) employs rectal examination during labor in the Obstetrical Clinic at the Hospital of the University of Minnesota. He claims for it certain advantages in that it is practically painless, there is no danger of septic infection, it is easy to perform, as it requires no preparation of the patient or doctor, and repeated examination by this method does not increase the danger of septic infection. Examinations can often be made more frequently than through the vagina, and thus the progress of labor can be more accurately followed. It also gives information concerning the full or empty condition of the rectum, and

the operator need not hurry in making the examination. Some abnormal conditions are recognized better by rectal examination than when a vaginal examination is made. Such would be the existence of a second, non-pregnant horn of a bicornute uterus. In certain cases of uterine tumor, as well as pregnancy, these tumors can be felt more readily through the rectum than through the vagina. Gloves should invariably be employed. An ordinary clean glove is usually sufficient. Mucilage of tragacanth should be used as a lubricant instead of vaselin, as it is easily washed off from the glove. Should there be any doubt concerning what is found by rectal examination it should be supplemented by vaginal examination. The writer has found this method useful, together with palpation in pregnancy and labor. Examination by the rectum should be an adjunct to that by the vagina, with the purpose of lessening the frequency of vaginal examinations. When a gauze sponge has been left in the vagina after an operation it can be detected by rectal examination because of the bulging. During the puerperal period this examination will detect retroversion of the uterus and also the degree of involution. In pregnancy it may reveal rectal carcinoma, fibroid, uterine tumors and abnormalities. One can also during labor observe the advancement of the head during a pain and thus get an idea of the progress of parturition. If the placenta has become detached and lies in the lower segment of the vagina this fact can be ascertained by rectal examination. When labor is delayed, and it is desirable to know how far the presenting part has advanced, by rectal examination the spines of the ischium can be detected and the position of the presenting part with reference to this landmark can be made out. Also after a difficult forceps delivery, rectal examination will detect fracture of the spines of the ischium or fracture of the coccyx. This examination also helps to determine the time when vaginal examination becomes absolutely necessary. It is sometimes possible in this way to increase the flexion of the head in delayed labor. It is thought that nurses should be instructed in this method, as thus they can more efficiently watch the progress of labor. The reviewer has never been convinced that rectal examination during labor was justifiable except in rare cases. No matter what precaution be taken the introduction and withdrawal of the finger or fingers into the rectum must transmit bacilli from the bowel to the region of the perineum. If palpation and auscultation are practised intelligently and in all cases the necessity for repeated vaginal examinations disappears. After delivery, when it is necessary to close lacerations of the pelvic floor, the highest point of these tears can often not be exposed unless the long finger of the gloved hand be introduced into the rectum and the pelvic floor strongly raised and drawn forward. This procedure is justifiable and is often of great service, but this should be done with the gloved hand only, and every precaution made to avoid the transference of material from the bowel upon the perineal region.

Germes Present in the Mouth and Rectum of the Newborn.—HYMANSON and HERTZ (*Am. Jour. Obst.*, April, 1917) have studied this subject in connection with germes present in the genital tract of the mother. They examined the secretions of the mother for bacteria and

also the secretions of the mouth and of the rectum of the infant. Of 42 cases so tabulated germs were found in 16 and none in 26. The staphylococcus was much more abundant than the streptococcus, and were the first to appear. Apparently the child becomes infected to some extent at the moment of birth.

Premature Separation of a Normally Implanted Placenta.—WING (*Am. Jour. Obst.*, March, 1917) describes 5 cases of this condition, in one instance the abnormality occurring twice in the same patient. The first patient was a multipara, a vigorous, muscular woman in good health. In the afternoon of the day before her admission to the hospital the patient ran up and down stairs violently a number of times. About midnight she began to have severe and steady pain in the abdomen and back. At nine o'clock on the following morning the patient suddenly passed a large blood-clot and a considerable quantity of fluid blood. This was repeated about an hour later. The patient was sent to the hospital; on admission her condition was poor, the uterus was very large and very firm, the os admitted three fingers, the membranes were intact, the vertex presented, partially engaged, and the heart sounds could not be heard. The child was delivered so soon as possible by version; the cord was around the body and hand of one arm. The placenta was almost completely detached and surrounded by a large quantity of clotted blood. The patient died in a few moments after delivery from hemorrhage and shock. An autopsy could not be obtained. A second case was that of a multipara who had worked very hard and was taken with pain in the abdomen and back which she thought uterine pains. On examination the cervix was obliterated, the os slightly dilated, the membranes intact, the breech presenting and the uterus was tonically contracted and very tender. The patient complained of constant pain in the uterus and severe headache. The fetal heart sounds could be distinctly heard. The general condition of the patient was fairly good. Four hours after admission external bleeding began. During the following six hours there was very little external bleeding, but at the end of this time the patient had a sudden and profuse hemorrhage. The membranes were ruptured and the uterus contracted promptly and expelled the child spontaneously. The placenta and a large mass of clotted blood followed the expulsion of the child. The uterus contracted normally and postpartum hemorrhage was absent. The child died on the second day and the mother made a good recovery. His third case, a primipara, aged twenty-two years, was from four to six weeks before her term. Twenty-two hours before admission to the hospital she fell heavily against the rim of the bath tub. This produced discomfort in the abdomen, and in three or four hours the patient had severe abdominal pain, with cramp-like exacerbations and severe backache. Vaginal hemorrhage gradually developed and, while not profuse, was constant. When brought to the hospital, twenty-two hours after the accident, the patient was nearly exsanguinated and mildly delirious. The cervix was unobliterated and barely admitted one finger. The placenta could not be felt. Abdominal hysterectomy was selected. Examination of the blood showed 33 per cent. hemoglobin. Just before operation, intravenous

saline transfusion was begun and pituitrin, ergot and morphin were given at the same time. Ether was used, a small amount only being required. The uterus was found firmly contracted and of a dark purplish-red color. There was no free blood in the peritoneal cavity. The placenta was almost completely separated; the uterus was merely emptied of its contents and the incision closed. The uterine muscle was softer than usual, deeper in color and infiltrated with blood. The uterine wound scarcely bled and the uterus contracted well. The patient was delirious following the operation, but finally made a good recovery in three weeks. Four months after leaving the hospital she again became pregnant. At the end of the seventh month she was taken with pain in the abdomen and brought to the hospital. The pain was so severe as to cause her to faint. On admission to the hospital she presented all the symptoms of severe internal hemorrhage, with tonic contraction of the uterus. Hysterotomy was performed through the former incision and on opening the abdomen it was found that the uterine incision had ruptured in its entire length; a placenta protruded through the rent. A seven months' fetus, placenta and membranes were at once delivered; the uterine scar was excised and the edges sutured in layers with chromic catgut. The uterus contracted well and the patient ultimately made a good recovery. Examination of the placenta showed a firm clot which had acted as a foreign body in separating the placenta from the wall of the uterus. On examining the excised tissues from the old scar no abnormality could be discovered. The writer also adds the case of a primipara who believed herself in labor because she had pain and who had slight bleeding from the vagina, which became copious. Placenta previa was suspected, and a physician called to the patient tamponed the vagina with iodoform gauze. On admission to the hospital her condition was fairly good. The fetal heart sounds could be heard, but the uterus remained tonically contracted and the cervix unobliterated and thick. Placental tissue could not be felt and the patient had a gestomino pelvis of moderate degree. Abdominal Cesarean section was performed so soon as possible, the uterus being found normal in color and appearance. Two coils of the cord were about the neck of the child, holding the neck and head close to the lower border of the placenta in such a way as to pull the edge of the placenta away from the uterine wall. Subsequent examination of the placenta showed separation over one-quarter of its area. The patient's puerperal state was satisfactory; she had no elevation of temperature, and mother and child made a good recovery.

Labor Complicated by Rupture of the Vagina with the Escape of the Fetus into the Peritoneal Cavity.—MATTHEWS (*Am. Jour. Obst.*, March, 1917) reports the case of a multipara brought to hospital by ambulance with the history that labor pains began abruptly in the early morning about three hours before, about the calculated time for confinement. Pains were severe for half to three-quarters of an hour, and suddenly, after a severe pain, the patient had no more. Considerable bleeding developed and almost immediately the placenta was expelled. A physician was summoned who ligated the cord and removed the placenta, and three hours later the patient was brought to the hospital.

On admission there was considerable shock and the abdomen was extremely large and markedly pendulous, with umbilical hernia protruding; the child was in the transverse position, with the head and right foot to the left, the back to the front and below the umbilicus. Above the umbilicus the soft parts were readily felt. The child was lying just beneath the abdominal wall and could be moved about readily. Its heart sounds could not be heard. On vaginal examination there was a large quantity of clotted blood, considerable fresh blood, and a protruding umbilical cord; the cervix could not be felt. When more clotted blood was removed a large tear was found in the posterior wall of the vagina. Operation was at once performed and, upon opening the peritoneal cavity, a full term fetus was found lying transversely in front of the uterus. There was a large quantity of free blood and clots. The dead child was removed, the blood clots removed so far as possible, when it was found that the uterus had not ruptured but that the tear in the posterior wall of the vagina, discovered by vaginal examination before operation, opened into Douglas' cul-de-sac, and from this opening the child had escaped backward and upward into the abdominal cavity. Supravaginal hysterectomy with clamps was quickly performed, iodoform gauze was placed over the cervical stump and carried down through the tear in the posterior vaginal wall out into the vagina. Several sutures were placed on either side of the gauze to close up the tear and prevent prolapse of the intestine into the vagina. The patient was in severe shock, from which she did not recover, and died twenty hours after the operation. A review of the literature of the subject shows very few such cases. Hart has pointed out the fact that the posterior vaginal wall is weak at its upper half, is more stretched during labor than the anterior wall and that rupture of the vagina is most common when the posterior vaginal wall is covered by peritoneum.

Hemolysis in the Transfusion of Babies with the Blood of the Mother.—CHERRY and LANGROCK (*Jour. Am. Med. Assn.*, February 26, 1916) draw attention to the hemorrhagic disease of the newborn and its usually fatal end. This can be divided into two classes: (1) in which hemorrhage may occur from the mucous membrane of the gastrointestinal tract, the stump of the cord and subcutaneously, in all of which the diagnosis is easily made because blood is seen, and (2) those cases of internal hemorrhage which are difficult to diagnose and exceedingly dangerous. The most successful treatment of this condition has been the injection of blood serum from the human or animal blood or the injection of whole blood. The writers have tried the transfusion of whole blood by using the mothers as donors. Preliminary hemolytic and agglutination reaction was obtained before using the mother as the donor for her child. The effort was made to establish the complete compatibility of the mother's and the infant's blood. Obviously, the mother would be the most convenient donor and usually available at all times. If it could be established that her blood was compatible to her infants it would save valuable time and prevent delay for making tests. After describing the technic employed the writers state that 34 tests were carried out on mothers and babies and that no hemolysis

or agglutination occurred. They therefore inferred that the blood of the mother may be used without tests for her infant. They narrate the case of an infant that had bleeding on the second day of life from the nasal mucous membrane, bowels, cord and kidneys. Without preliminary test the infant was given 60 c.c. of the mother's blood through its external jugular vein by the indirect syringe method. One hour after transfusion no bleeding occurred from the wound made over the vein, and three hours later the stools were free from macroscopic blood and there was no other bleeding from any portion of the body. It has been estimated that the volume of blood possessed by the infant is one-twentieth of its body weight. In an infant weighing seven pounds its blood would be approximately $5\frac{3}{8}$ ounces. It is well-known that if one-third of the entire blood supply is lost by hemorrhage there is grave danger of death. It is important to know how much blood to use, for if too much be thrust into the circulation the heart muscle may suddenly dilate and death occur. It is estimated that from 60 to 75 c.c. of blood is approximately sufficiently to supply the infant with the necessary elements to promote clotting and enough cellular elements to replace those lost by bleeding. This is an important reason why the indirect method of transfusion should be practised in infants as well as the simplicity of the technic.

Thymus Death.—FALLS (*Surg., Gynec., and Obst.*, June, 1916) describes the case of a primiparous woman, aged twenty-four years, with normal labor terminating spontaneously in thirty-six hours. The baby breathed without difficulty until about two hours after birth, when respirations were difficult and the child cyanotic. This condition lasted for two hours, when the cyanosis deepened, respiration became more difficult and the child died without convulsions. Before and after birth its heart sounds were normal; just before death the pulse went down to thirty per minute. At autopsy the skin of the head, neck, arms and thorax was red and congested. The head showed no signs of trauma. The pericardial sac contained a large amount of serosanguineous fluid and the left lung was compressed and pushed to one side by a large thymus 4 cm. broad at its widest part and 5.5 cm. long. Crossing the upper portion of the thymus, from left to right at the upper border of the clavicle to the level of the lower border of the first rib, was the left innominate vein. This had compressed the thymus and lay in a groove on its surface. A branch of this vein leaves the thymus tissue at about the midline of the body. There was no evidence of thrombosis in the thymic veins, the left innominate or superior vena cava. There was edema of the posterior portion of the lung, more marked on the left side, and there were small hemorrhages on the substance of the kidney. Histological examination made of the hypophysis, thymus, thyroid, adrenal and spleen revealed no abnormalities. The trachea was opened just above the upper edge of the main portion of the gland. There was evidence of compression of the trachea by the main body of the thymus, as shown by the difficulty in passing a probe down upward from the opening. The anomalous vein in this case was the left innominate. This is normally situated posterior to the thymus and joins the right innominate to form the superior vena cava. It is

difficult to assign exactly the cause for death. Undoubtedly, the pressure of the thymus gland upon the trachea and upon the surrounding vessels was the main factor in the case.

Cesarean Section through the Lower Uterine Segment.—COSTA (*Jour. semaine méd.*, 1916, xxii, 552) dates this method to Jorg, of Leipsic, in 1807, and Osiander, Ritgen, in 1821, demonstrated the extraperitoneal method. In 1870 Thomas, of New York, published his paper on the subject. In 1907 there were before the profession seventeen distinct operations. The author divides these into extraperitoneal and transperitoneal. The first was founded on anatomical study, but the second arose from the fact that during the performance of an operation it was often impossible to make the operation an extraperitoneal one. Franck published his first 7 cases in 1904 and Selheim, Latzko and others have improved the method. Accidents are more numerous by the extraperitoneal route, and it is estimated that the peritoneum is opened in about 20 per cent. of cases. Next in frequency is injury to the bladder in 3 per cent. Fixation of the uterus to the abdominal scar has been observed, and this facilitates uteroflexion. Such adhesions are present in about 25 per cent. of the cases but do not always cause dystocia in subsequent labor. Many believe that the principal indication for section through the lower segment is presence of infection, and when one remembers how readily the peritoneum is opened and communication thus established with the peritoneal cavity it becomes evident that in cases of infection this is not the safest method. Selheim treated 6 cases of placenta previa and Hinkel 1 without entering it. Most operators, however, believe that this method cannot compare with delivery through the vagina in appropriate cases nor with the classic Cesarean section. It is thought that conditions which contra-indicate the classic section, such as threatened rupture of the uterus, incomplete rupture of the lower segment, pulmonary tuberculosis, meningitis and pelvic tumors, indicate the operation. The writer believes that after this operation the scar is better and there is less likelihood of rupture of the uterine scar in subsequent confinements than after the classic section. The best statistics of maternal mortality give 5.33 per cent. with an operative mortality ranging from 4.2 to 2.85 per cent. Postoperative complications occur in about 30 per cent. Fetal mortality varies from 1 to 3.62 per cent. Statistics would indicate that the section had an advantage of about 2 per cent. in mortality over the classic section, but many believe that this apparent advantage occurs because the classic section is performed with faulty technic.

Induction of Labor for Pelvic Deformity.—GUICCIARDI (*Annal. de Ostetricia*, 1916 No. 2) writes with discrimination concerning this subject and describes cases in which Cesarean section was chosen in preference to the induction of labor for pelvic deformity, and also points out the various methods which are permissible in this complication. The tendency is to do away with the induction of labor in the interest of the child and to substitute for it the performance of one of the other obstetric operations. A spontaneous expulsion of the fetus

is, of course, the ideal solution, and this may sometimes be aided by exercise during the last months of pregnancy, and success may be hoped for in cases of slightly contracted pelvis. The use of the forceps is permissible when once dilatation proceeds successfully and the head engages. Embryotomy upon the living fetus in good condition is now declined by obstetricians, and so are all methods which deliberately sacrifice a child in good condition. Cesarean section, to be successful, should be made as greatly elective as possible and care taken to select those patients who have not been previously repeatedly examined and in whom efforts at delivery have not been made. Pubiotomy has many claims made for it, but its field is evidently a limited one. When there is doubt as to whether the child can pass through the pelvis one may employ the test of pressing the fetal head gently into the pelvic brim. Attention is called to the many varieties of Cesarean section now perfected, and the statement is made that the operation must be appropriate and useful.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Two-stage Operation for Carcinoma of the Pregnant Uterus under Paravertebral Anesthesia.—While all operators are in accord that carcinoma of the pregnant uterus is an extremely grave complication, MASON and KONRAD (*Surg., Gynec. and Obst.*, 1918, xxvii, 75) are of the opinion that by a two-stage operation under paravertebral anesthesia shock may be greatly reduced and frequently the life of both mother and baby saved. In a careful review of the literature they failed to find a single case in which a radical cure had been undertaken in a two-stage procedure; in most instances the child was delivered and the uterus extirpated at the same time or, the tumor being inoperable, the child delivered by the abdominal route. According to the authors the extreme vascularity of the entire pelvis at the time of delivery makes a careful pelvic dissection difficult, if not impossible, the condition of the patient at that time necessitates haste which is often incompatible with thoroughness, and hence the chances of recurrence are increased. They therefore advocate that a Cesarean section be performed at the first sitting and that the hysterectomy be undertaken at a second laparotomy after the patient has recovered from the shock and loss of blood incident to delivery, the intervening period being short and never extending over the complete uterine involution. As a further means of diminishing shock, both procedures may be carried out under paravertebral anesthesia. They observed no untoward general reactions, and anesthesia lasted from two to four hours. In the authors' case twenty-two days were allowed to elapse between Cesarean section and hysterectomy. The patient's life was undoubtedly prolonged

by the two-stage procedure, but the extent of the growth even at the time of the first operation made ultimate recovery impossible, death occurring four and a half months after delivery.

New Operation for Prolapse of the Uterus.—A new operative technic has been devised by COLLINS (*Surg., Gynec. and Obst.*, 1918, xxvii, 326) for cases of complete prolapse of the uterus in which the uterine ligaments have so lost their elasticity that the organ remains outside the body even when the patient is lying down. Since the majority of patients requiring this operation are elderly women with long-standing bladder derangement, Collins recommends that they be under observation for some time prior to operation, during which time the power of the kidneys to withstand the sudden relief of backward pressure through complete emptying of the bladder should be carefully tested. This is done by suspending the uterus high in the pelvis with a gauze tampon and introducing a Pezzer catheter in the bladder for several days preceding operation. This may be done several times if satisfactory results are not obtained the first time. The technic of the operation is briefly as follows: A transverse Pfannenstiel incision is made over the pelvis through the aponeurosis of the recti muscles, after which a parallel incision is made two and one-half inches long and one-fourth inch above the first, thus forming a strip of aponeurosis with natural attachments at either end. The recti muscles are then separated, the peritoneum incised longitudinally and a supravaginal hysterectomy performed, removing a V-shaped piece out of the cervix and thus leaving an anterior and posterior flap on the cervix. The broad ligaments may usually be lighted *en masse* in these cases. The two cervical flaps are then held forward and the stumps of the broad ligaments sutured to each other and to the posterior surface of the cervix. At this juncture the cervical flaps are held apart, the strip of aponeurosis dropped in the cervical trough which has been formed and the flaps sutured over the strip. The peritoneum and recti muscles should be sutured around the cervix while the edges of the aponeurosis are sutured over the cervical stump and the supporting strip of aponeurosis. This method, the author feels, is preferable to Kocher's, inasmuch as no large pieces of uterine tissue are left in the abdominal wall between the aponeurotic and muscular layer and because suspension is accomplished by a normally attached strip of aponeurosis and the union of similar dense structures over this strip.

Bloodless Repair of the Cervix.—After experimentation with various kinds of clamps and tourniquets HEINEBERG (*Am. Jour. Obst.*, 1918, lxxvii, 652) has devised the following technic for bloodless repair of the cervix uteri: (1) Introduce a self-retaining speculum in the vagina. (2) Grasp the anterior lip of the cervix in the median line with an ordinary double tenaculum. (3) Dilate the cervix moderately, chiefly to determine the precise location and direction of the canal. (4) Draw the cervix toward one side and apply the angulated forceps to the cervix well above the level of the proposed amputation or denudation. (5) Draw the cervix to the other side and apply the second angulated forceps opposite the first one. (6) Remove the ordinary tenaculum.

(7) Place the handles of the forceps together. Stretch the rubber ring over them and push it up on the cervix to above the retaining balls. (8) Separate the handles of the forceps and hand them to the assistant. Hemostasis is thus maintained by the use of a rubber ring and two tenaculum forceps which, in addition to being angulated, possess a pedunculated ball on the outer aspect of each blade just above the angle, the balls holding the rubber ring in such a position that it compresses the cervix above the grasp of the forceps.

Obstructive Dysmenorrhea and Sterility: a New Operation.—While the original Pozzi operation meets all the requirements in cases of true "pin-hole" os where the obstruction is at the external os, there are many cases in which angulation of the uterocervical canal near the internal os is responsible for the dysmenorrhea and sterility. It is in the latter cases that FRANK'S (*Jour. Am. Med. Assn.*, 1918, lxx, 985) operation, by which the cervical canal is straightened and the stenosis at the internal os corrected, is particularly applicable. The cervix is grasped at the uterovaginal junction with small uterine tenaculum forceps, one on each side, and pulled outward and upward. An incision is made in the middle of the posterior lip extending well up to and past the flexion. At this point the tenacula are removed and used to spread apart the two halves of the posterior lip. With a very small-bladed, spear-shaped knife, made on the Catlin order, wedges of tissue are removed from the two raw surfaces of the posterior lip, leaving a trough. Just enough tissue is then removed to allow easy and exact approximation of the entire cervical and vaginal surfaces. The first suture is commenced at the angle of the posterior incision and extreme care taken to approximate accurately the internal cervical and the vaginal mucosa at this point. This is important, to avoid healing by granulation and so secondary contraction. Twenty- or forty-day No. 1 chromic gut is used in a continuous or interrupted suture. Frank suggests that the principle of this operation might be applied in cases of retroflexion of the uterus producing symptoms.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH,
PITTSBURGH, PA.

Significance of the Cartilage in a Carcinochondrosarcoma of the Mouse.—It is not uncommon to find a sarcomatous change of the stroma in both spontaneous and transplanted carcinomata of the mouse, though rare in rats, dogs and man. However a few such cases have been reported, only 3 in rats, 1 in a dog and 28 in man. This sarcomatous transformation is regarded by most authors as a change

in the connective-tissue framework of the tumor in response to some special stimulation exerted upon the stroma by the epithelial portion of the tumor. Others refer to it vaguely as a chemical agent, and still others attribute the change to a parasite living in symbiosis with the carcinomatous cell. Krompecher denies that the change is in the connective tissue and insists that the epithelial elements have assumed a spindle shape. WOGLOM (*Jour. Cancer Research*, 1918, iii, 47) offers new observations in favor of the hypothesis that the spindle-shaped cells of the type of growth ordinarily called carcinosarcoma are of connective-tissue origin. In a transplantable mouse, carcinoma which temporarily possessed the power to produce the sarcomatous transformation in its stroma, cartilage was discovered in at least three of the four mixed growths in the second generation. The usual explanation of such a finding would be that a portion of costal cartilage had been involved by the tumor during its growth and had been removed with it. Serial sections, however, proved that this was not the case; many independent islands of cartilage, some composed of only a few cells, lay scattered through the stroma, and, furthermore there was a very gradual transition between these cartilaginous areas and the surrounding sarcoma. The only remaining explanation is that this cartilage is a product of the spindle cells surrounding it. As it has never been proved that mature epithelial cells can produce cartilage, and as, on the contrary, it is known that connective-tissue tumors are able to form cartilage, it seems safer to assume that any cartilage within a tumor has had its origin from the connective-tissue elements. Further evidence is brought to bear by Haaland, who found intra- and intercellular fibrils in the sarcomatous parts of mixed neoplasms and also by Slye, Holmes and Wells, who regard the presence of myxomatous degeneration in one of their tumors which resembled the mixed growths as suggestive of sarcoma. As cartilage was never found in the stroma of the pure carcinoma under consideration it is obvious that interpolation of the sarcomatous transformation was one of the conditions necessary for the emergence of this metaplasia. It seems more probable that the cartilage emerged by differentiation of the connective tissues than that embryonal remnants of cartilage were present.

Growth of Tumors in the Chick Embryo.—With the discovery by Murphy that the chick embryo might be used as soil for the growth of foreign tissues, it appeared that it might prove to be a medium for the growth of human neoplasms as well as for transplantable tumors of animals. STEVENSON (*Jour. Cancer Res.*, 1918, iii, 63) reports the results of experiments undertaken to determine any differences that may occur between tumor growths in the original species and in the chick embryo. The investigations included the study of tumors of different growth rates, a comparison between early stages of tumor grafts in the chick and in the original species and the effect of prolonged residence in the chick upon the growth of a mouse tumor and its behavior when returned to the animal. The experiments were made with eggs from one dealer, but were not all from the same breed of fowl. The eggs were incubated and inoculations made on the fifth to the eighth day of incuba-

tion. The tumors grew in about 30 per cent. of the total number of eggs used. As to growth rate it was discovered that tumors growing in the chick embryo preserve approximately the same rate that they exhibit in the original animal. This means that such a medium when used for experiments that must continue for more than one generation becomes limited to the more rapidly growing tumors, as it is only with these that sufficient tumor could be produced for further inoculations. Furthermore, there was no evidence of either retardation or stimulation of the growth rate of a tumor in this medium. Animal tumors seem to assume exactly the same size in the chick embryo that they did after proliferating an equal length of time in the original animal. However, there is little hope of being able to maintain a tumor of slow growth indefinitely in the chick. In the latter the chick exerts an unfavorable influence upon tumors growing in it, as seen by the growth of a mouse tumor in a chick and its behavior upon being returned to the mouse. This is probably due to a lack of suitable nutritive material rather than to an active immunity, for upon repeated transplantation areas of necrosis were seen scattered throughout the tumor. Microscopic studies displayed the fact that tumors tend to preserve not only their morphology but their power to recover antecedent characteristics, and they grow in symbiosis with the chick tissue as readily as they do with those of the original animal.

Study of Heterologous Tumor Grafts.—Considerable attention has been given the presence of lymphocytes in the vicinity of human tumors. It has been a common observation that lymphocytes appear in greater or less number around carcinomatous masses. But only recently has the presence of these cells been interpreted in terms of immunity. Some believe that the local resistance to tumor invasion is in direct proportion to the numbers of lymphocytes and plasma cells. Some even go so far as to give a numerical interpretation of the tumor resistance by a histological study of tissues. Just in what manner the lymphocytes are able to produce a local immunity or even, as some claim, are effective in destroying the implanted tumor has not been explained. BULLOCK and ROHDENBURG (*Jour. Cancer Research*, 1918, iii, 31) carried out a series of experiments upon mice, using two carcinomata and two sarcomata for inoculation. Ten to fourteen days after subcutaneous inoculation the grafts were excised and studied microscopically. The mouse tumors were inoculated into rats and one rat tumor inoculated into mice. A great number of animals were used. From their studies the authors draw the following conclusions: "While the death of some heteroplastic tumor grafts may perhaps be attributed to the action of lymphocytes and connective tissue, there is no histological proof that it is always determined by these factors. Tumors elicit in foreign species a reaction of much the same character as that produced in homologous animals. Removal of the spleen has no influence upon the receptivity of an animal toward heteroplastic tumor grafts. Splenectomy does not favor the growth of heteroplastic tumor grafts. One inoculation of a heterologous tumor does not always render an animal immune to the temporary growth of a subsequent heterologous graft."

Phagocytosis in Vivo under Various Conditions.—Interest has always surrounded the question as to the manner in which bacteria are removed from the body. Inferences upon the solution of the problem have been gained through the *in vitro* tests. The results of the numerous investigations upon the bacteriolytic and opsonic qualities of the serum have been inadequate when applying the findings to the living animal. Bull has directly called our attention to the differences in the *in vitro* and *in vivo* findings particularly in regard to the pneumococcus and the *Bacillus typhosus*. With the former it was shown that an active antipneumococcus serum caused an agglutination of the pneumococcus *in vitro* and *in vivo*, but that the actual disappearance of the microorganism from the blood results through rapid clumping of the cocci and the removal of these clumps by the liver, spleen and lungs. By subsequent work with typhoid bacilli he found that these microorganisms are promptly agglutinated in the circulating blood of normal rabbits and quickly removed from the blood stream by the liver and spleen. These bacteria in their agglutinated state are taken up by leukocytes and destroyed. He further observed that similar results *in vivo* could be obtained with the bacillus of dysentery and influenza, the *Staphylococcus aureus* and *albus*, the meningococcus and gonococcus. Subsequently, Bartlett and Ozaki carefully followed the fate of the *Staphylococcus aureus* after injection into the circulation of dogs. They found that these microorganisms are almost immediately removed from the circulation and stored in relatively large numbers in the lung capillaries, where they are ingested by polymorphonuclear leukocytes. The bacteria were also found to accumulate in the liver and spleen, but their presence in these organs appeared to be associated with the diminution in the numbers found in the lung. The bacteria completely disappear from these organs within forty-eight to fifty-two hours. The kidneys do not appear to play an important role in removing the bacteria from the blood stream, but infection in them is a secondary process, with a chance that a destructive invasion will occur after a period of adaptation. BARTLETT and OZAKI (*Jour. Med. Res.*, 1917, xxxvii, 139) have lately elaborated their studies upon this problem and offer further information regarding the fate of bacteria *in vivo*. The previous experiments had attracted attention mainly to the polymorphonuclear leukocytes as the active agent in removing bacteria from the blood stream. These findings showed some discrepancies when leukocytic activity was determined by *in vitro* experiments. Animals were injected with cultures of the *Staphylococcus aureus* and killed ten minutes after inoculation. The organs were rapidly fixed and then stained for bacteria, attention being particularly paid to counts indicating the number of microorganisms ingested by various types of cells. In the different experiments animals were placed under various abnormal but non-infectious conditions, which might modify the phagocytic action of the leukocytes or of the fixed cells. Observations were made upon the animals subjected to chloroform, fasting and phosphorus poisoning. It was observed that anesthesia had no marked influence on the phagocytosis of the leukocytes *in vivo*, but that acute phosphorus poisoning caused some diminution in the leukocytic activity. A marked decrease in phagocytosis was

observed in the presence of an advanced acute general infection by the *Staphylococcus aureus*. On the other hand an acute infection by the *Bacillus coli* had no effect upon the phagocytic activity of leukocytes for the staphylococcus. When the leukocytes show less avidity for phagocytizing bacteria the fixed tissue cells of lung and spleen and liver show a greater degree of phagocytosis. The response on the part of these cells is looked upon as a compensatory measure to balance against activity on the part of the leukocytes.

Elaboration of Specific Soluble Substance by Pneumococcus during Growth. — DOCHEZ and AVERY (*Jour. Exp. Med.*, 1917, xxvi, 477). Cell-free fluids of young cultures of pneumococcus contain a specifically reacting substance of bacterial origin. This substance is present when the organisms are growing at their maximum rate and undergoing little or no cell death, and consequently its presence is not dependent upon cell disintegration but represent the extrusion of some bacterial substance by the living organism. The urine very frequently, and the blood more rarely, of rabbits experimentally infected with pneumococcus contain a similar specific soluble substance during the early hours of the infectious process, which substance is easily demonstrable by the use of homologous immune sera. Human beings suffering from lobular pneumonia have in their blood and more frequently in their urine a specific soluble substance of pneumococcus origin. The amount of this substance present in the urine varies in different individuals and the presence of a large amount is of unfavorable prognostic import. The frequency of demonstrable precipitin reactions in any given case depends upon the strain of the pneumococcus infection and whether or not the patient is receiving the serum treatment. This specific precipitin reaction in the urine is of diagnostic value. Rabbits injected with soluble pneumococcus material continue to excrete this substance for a considerable period of time. The specifically soluble substance obtained from bacterial cultures and from the urine during infection is not destroyed by boiling, by precipitation with alcohol, acetone or ether or by trypsin digestion. Studies are in progress on the degree of toxicity and on the antigenic properties of the substance.

Neutralization of Antipneumococcus Immune Bodies by Infected Exudates and Sera.—COLE (*Jour. Exp. Med.*, 1917, xxvi, 453). In empyema fluids resulting from infection with pneumococci there are present large amounts of soluble substance which have the property of neutralizing pneumococcus antibodies. Similar substances are found in the blood of infected rabbits. When immune serum is injected into infected rabbits the immune substances disappear very quickly and therefore are prevented from actively overcoming the infection. When immune serum is administered to patients severely infected with pneumococci the immune bodies may also disappear very rapidly, and this disappearance is probably associated with the presence of such soluble substances in the blood. The serum only becomes effective when these substances are neutralized. The study of agglutination curves is of value in showing why in certain instances favorable results have not

followed the use of immune serum. In all cases treated with serum Type I agglutinins can be demonstrated in the patient's blood two to three minutes after the administration of 75 to 100 c.c. of serum. With the rise of the agglutinating power the temperature curve falls. Serum treatment must be active at the start. It is important to give large doses of immune serum at the beginning of the treatment. Studies of agglutination curves in the cases of Type I infection do not give definite proof that the effect of immune serum is limited by the presence of soluble substances in the blood.

Further Studies on the Epidemiology of Lobar Pneumonia.—STILLMANN (*Jour. Exp. Med.*, 1917, xxvi, 513). Pneumococci of Type I and Type II are responsible for the majority of the cases of lobar pneumonia while those of Type III and Type IV produce the rest of the cases. Among the pneumococci found in the mouths of healthy individuals Type IV predominated, Type III is frequent and atypical organisms of Type II are occasionally found. Healthy persons intimately associated with cases of lobar pneumonia may harbor in their mouth secretions the highly parasitic pneumococcus of Type I and II. The time interval involved in this association is a variable quantity. In the majority of contact carriers the organism isolated from the mouth corresponds strictly to the type of organism found in the infective cases. Occasionally a carrier of Type I or Type II pneumococcus is encountered in whom it is impossible to trace any contact with an infected patient. From the dust of homes where cases of pneumonia due to Types I and II have occurred, pneumococci of the same type may be recovered. Air-borne infection may play a part in the production of pneumonia. The mere presence of disease-producing pneumococci in the mouth will not initiate infection, susceptibility of the individual being a prerequisite.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE,
WASHINGTON, D. C.

Study of Diphtheria Carriers.—LEWIS (*Boston Med. and Surg. Jour.*, May 2, 1918, p. 602) states that there are two factors which should make this subject timely: (1) the unappreciated known fact that measles is followed by diphtheria; (2) that a so-called experiment based on

certain knowledge of the first factor has given rational results as well as demonstrating what should be the simplicity of control of the disease. From his studies Lewis concludes that the continuous search for carriers in controlling diphtheria is an exact sanitary measure of prevention. All individuals with acute catarrhal nasal conditions are the potential acute nasal diphtheria carriers; it requires the presence of a chronic carrier, generally also nasal in type. The permanency of the former when made a carrier is dependent on the degree of nasal obstruction. All individuals convalescent from any respiratory disease, however mild, constitute the largest proportion of nasal carriers of diphtheria. Investigation of all such individuals and their isolation, if carriers, is the essential basis of control of diphtheria. In general, cases follow the production of acute nasal carriers by chronic ones. Responsibility for any frequency of the disease is solely that of health authorities.

Are All the Tubercle Bacilli Found in the Sputum Virulent?—CORPER (*Jour. Am. Med. Assn.*, May 4, 1918, p. 1281) states that it was deemed advisable to investigate the problem of the virulence of tubercle bacilli in the sputum of consumptives on account of the lack of conclusive available data and the tremendous importance of this information for the institution of hygienic measures in preventing and eradicating the disease. His investigations revealed that in the majority of open cases of pulmonary tuberculosis the tubercle bacilli which could be isolated on artificial mediums from the sputum were virulent enough to produce systemic tuberculosis in guinea-pigs by means of doses as small as 0.000001 mg., and that the range of variation was very small, as was also pointed out by Gilbert and Gregg, who found it to lie between 10 and 120 bacilli. The author further states that if the virulence of the bacilli as cultivated on artificial mediums is a direct expression of their virulence in the sputum there is only one conclusion to be drawn from the foregoing findings, as viewed from a practical stand-point, and that is, that in open cases of pulmonary tuberculosis the tubercle bacilli discharged by droplet or by expectoration, when still uninfluenced by drying and light, are a danger to mankind through direct transmission at least. In applying these findings to mankind there was found in the literature only one reference which would indicate the relation between the number of bacilli of the same culture necessary to infect a guinea-pig and to infect man. These observations were made by Webb and Gilbert, who found that a culture of human tubercle bacilli sufficiently virulent to infect a guinea-pig when ten bacilli were used was also capable of infecting a child in practically the same dose. It seems justifiable therefore to conclude that the tubercle bacilli found in the sputum of patients in open cases of pulmonary tuberculosis (provided the bacilli capable of artificial cultivation are a true index of those existing in the native sputum) vary only slightly in virulence for guinea-pigs, and are for practical purposes nearly all pathogenic. That is, in 97 per cent. of the cases they will infect a child, as may be deduced from Webb and Gilbert's observations, in a dose of less than one-millionth milligram. These experiments also seem to lay special emphasis on the examination of the sputum of men in military service or about to enter it.

Meningococcus Carriers: Preliminary Report from First Naval District.—REDDEN (*Boston Med. and Surg. Jour.*, May 9, 1918) states that meningococcus carriers in this district have been isolated on the basis of agglutinations in $\frac{1}{10}$ or $\frac{1}{50}$ dilutions of polyvalent antimeningococcus sera on slides, followed by gross agglutinations in tubes, the final readings being taken after twelve hours in the incubator at 55° C. and twelve hours in the ice-box. This has been supplemented by a careful study of cultural characteristics. Over three thousand cultures have been examined, of which about three hundred have been positive for meningococci. Of this group about 40 per cent. agglutinated specifically in $\frac{1}{10}$ antimeningococcus serum, and about 60 per cent. as high as the $\frac{1}{50}$ dilution on the slide. Experience has shown that results of gross agglutination in tubes rarely alters the positive findings obtained on slides. Repeated examinations of a group of 100 carriers showed that only 16 per cent. were ready for discharge at the end of the minimal isolation period of two days; that 7 per cent. remained positive over forty days; that 6 per cent. showed positive cultures after three successive negatives; that 49 per cent. showed positive cultures after one or more negatives, thus demonstrating a persistent and an intermittent type of carrier; that a carrier may show a pure culture of meningococci on one examination, on the next only a few scattered colonies in a mixed culture and on the third a pure culture of meningococci. Treatment has been of no value in our hands. A sharp decline in the number of positive cultures from the carrier group has been noted during the past two weeks of warm weather. A study of 13 groups of so-called "contacts" and 6 groups of "non-contacts" brings out the following facts: Under good hygienic conditions, groups of naval men in this district, if only moderately well selected on the basis of possible contact with a known case of cerebrospinal fever, show from 6 to 8 per cent. carriers. If hygienic conditions are poor, that is, if men are in crowded quarters, are subjected to severe physical labor under extremes of heat and cold, such groups may show from 17 to 22 per cent. carriers. Among groups of naval men well selected on the basis of possible contact with a known case of cerebrospinal fever and living in close contact with each other either on shipboard or in crowded quarters 20 to 35 per cent. appear to be carriers, the upper limit representing the most carefully chosen group. But when only a small group of guards isolated from the rest of a crew is considered only 11 per cent. appear positive. One group of 100 men taken at random from a camp where there had been no case of cerebrospinal fever, and where living conditions are excellent, showed 9 per cent. carriers as contrasted with 26 per cent., which appeared in a group of 100 taken from barracks where men were decidedly overcrowded and from which a number of cases had been taken, also, where 20 to 25 per cent. carriers had been found on previous examinations. Another non-contact group of 79 men, representing a naval student body living in barracks under good hygienic conditions, showed 9 per cent. as contrasted with the 1 per cent. found among 100 women students of Simmons College and the 1 per cent. found among the first and second-year Harvard medical students. In these last three groups about all the factors were common, but the naval group ate at a common mess

and lived in barracks, whereas the others lived chiefly at home or in small groups. Hence it is evident that the important factors which change the number of carriers from as low as 1 to 2 per cent. among civilians to as high as 20 to 35 per cent. among recruits are: contact with known cases of cerebrospinal fever; unhygienic conditions such as come from crowded barracks; severe physical labor, coupled with exposure to extremes of heat and cold; and, finally, contact with carriers of meningococci.

Increasing Mortality after the Age of Forty-five; Some Causes and Explanations.—DUBLIN (*Quarterly Publication of the American Statistical Association*, March, 1917) states that the apparent increase during recent years of the death-rate after the age of forty-five has caused many statisticians and health officers to fear that changes in conditions of life in this country have reduced the expectation of life at the higher age groups. He has shown on the basis of statistics for New York State that this fear is ungrounded and that the increase is in large measure, if not entirely, due to another factor that has been heretofore neglected, *i. e.*, to the effect of changes in the racial composition of the population. He shows that the proportion of the native born in each ten-year age period after forty-five has decreased in recent years and that, correspondingly, the proportion of the foreign stock at these age periods has increased. He then shows that without exception the death-rate in the older groups is higher among the foreign born and the native born of foreign parentage than among the native born. This means that in the older age groups of the population there has occurred in recent years "an increase in the proportion of those having higher death-rates and a corresponding decrease in the proportion of those having lower death-rates," a change which "must have had the effect of increasing the total death-rate" at these ages. The increase in the death-rate from cancer, Bright's disease, heart diseases, diabetes and the other so-called degenerative diseases that are largely responsible for the mortality after the age of forty-five is partly to be accounted for on similar grounds, since the death-rate from these causes is higher among the foreign than the native born. The increase in mortality from these diseases, however, is also partly to be accounted for by certain changes in the methods of certifying and tabulating causes of death in statistical offices, which have resulted in an increase in the published though not in the actual death-rates from these diseases. Americans today, according to the author, are not experiencing a shorter expectation of life after the age of forty-five than did Americans of a previous generation.

Flight of Mosquitoes.—LE PRINCE (*U. S. Public Health Reports*, May 4, 1917) states that in the Southern States *Anopheles quadrimaculatus* is probably the principal carrier of malaria. The extent to which *Anopheles punctipennis* or *Anopheles crucians* may transmit the disease has not yet been determined. In connection with malarial investigations on impounded waters in 1914-15 opportunities were afforded to determine how far from known breeding places anopheles could be found. Numerous inspections of the interiors of buildings

indicated that *Anopheles quadrimaculatus* was very rarely present more than a mile from the breeding area, even though the latter was very prolific. This species was never found in houses and barns located at distances of $1\frac{1}{4}$ miles and more from the most prolific breeding places. Persons living $1\frac{1}{2}$ miles from such areas reported an entire absence of mosquitoes. The experiments were planned on the same lines as those carried out with the flight of a Panama species, *Anopheles tarsimaculata*, at Gatun. Accordingly a number of *Anopheles quadrimaculata* were captured alive for the test, the sources from which they were taken and the methods of capture being as follows: (1) Mosquito nets were placed close to the breeding places at night and the anopheles were attracted into the nets by men who served as bait. The anopheles were stained in the nets by spraying with a 1 per cent. aqueous solution of eosin (yellowish) from an atomizer and liberated. (2) Resting anopheles were caught in heavily infested houses in the daytime by means of a hand-collecting device. The mosquitoes were taken to a point in the breeding area which had been selected as a liberation station. They were then stained as above described and allowed to escape. On the first day only a few were set free, but on the second day a large number was liberated, all at one point. The author concludes that the flight of *Anopheles quadrimaculatus* in nature extends to approximately a mile from a breeding place producing very profusely. Beyond this distance stained specimens were not found. The distance of flight from a place producing very freely, but less profusely than some, was approximately a half-mile. Stained specimens of *Anopheles quadrimaculatus* were taken as follows: 1 at 5565 feet from the point of liberation; 2 at 3245 feet; 3 at 3090 feet; 1 at 2800 feet. *Anopheles quadrimaculatus* in one test flew across a river 800 feet wide in returning to a plantation from which they were originally caught for the test. Approximately 900 to 1000 mosquitoes were liberated.

Drinking Fountains.—WHITTAKER (*U. S. Public Health Reports*, May 11, 1917) investigated 77 drinking fountains in use at the University of Minnesota. These fountains represented fifteen different types, all of which were found to be improperly constructed to prevent them from contamination by the consumer. The bacteriological examinations conducted on these fountains showed that 80 per cent. of these fountains contained streptococci when they were not found present in the water supplied to the fountains. These results indicate that drinking fountains may be a factor in the transmission of communicable diseases, a condition which should be remedied. Experiments were conducted with various types of fountains to supplant those in use and a type was designed which is stated to be both economical and safe from a sanitary point of view. It was found necessary, in a practical design, to entirely protect the point of discharge and to guard the nozzle against the approach of the consumer. The nozzle in this design fulfils these requirements and can be substituted for the nozzle used on practically any of the common types of drinking fountains. This type of nozzle protects the point of discharge by enclosing the small discharge tube in a larger tube, which is cut at an angle, with its upper surface extending

beyond the outer extremity of the inner tube. The wire muzzle prevents the consumer from approaching the point of discharge. This nozzle can be used on the constant or intermittent flow type. In cases in which the water-pressure varies to a large degree pressure regulators should be installed. Doubtless there are many other mechanical possibilities of accomplishing the same result, but the one designed is simple and inexpensive and it can be attached to practically any fountain.

Anopheles Punctipennis; a Note on its Ability to Serve as a Host for Plasmodium Falciparum.—MITZMAIN (*U. S. Public Health Reports*, July 6, 1917, p. 1081) states that the experimental determination of the role of *Anopheles punctipennis* as a potential host for the common forms of malaria has been established, as ascertained by King. No additional findings have been developed whereby previously reported negative results with this anopheline and *Plasmodium falciparum* might be accounted for. In the present series 52 specimens of *Anopheles punctipennis* were fed upon the blood of cases of subtertian malaria, and 14 infections resulted. Of 8 specimens of *Anopheles quadrimaculatus*, used as controls under identical conditions, 4 became infected. *Anopheles punctipennis*, while highly susceptible to infection with *Plasmodium vivax*, exhibits no special predilection toward this species, but it has been shown to be a sufficiently receptive host of *Plasmodium falciparum* to be held of sanitary importance. From the writings of Beyer and his co-workers, Craig and others it has been concluded that a specific relation exists between American anophelines and the several varieties of malaria. The transmission of tertian and quartan malaria has been held to be effected by *Anopheles quadrimaculatus*, while to *Anopheles crucians* has been ascribed the incidence of subtertian malaria. Craig concluded that: "The observations noted explain clearly why certain localities suffer more severely than others from certain types of malarial infections. Given a locality in which only *Anopheles crucians* occurred and we could have nothing but estivo-autumnal infections; but if *Anopheles quadrimaculatus* were the only anopheles present we might have either tertian or quartan infections but no estivo-autumnal malaria." The present status of the common American anophelines with reference to their susceptibility to infection with the several species of malarial parasites is as follows: *Anopheles quadrimaculatus* may serve as a host for all three parasites of malaria. *Anopheles punctipennis* and *Anopheles crucians* are susceptible to infection with *Plasmodium vivax* and *Plasmodium falciparum*.

Intravenous Injection of Typhoid Vaccine.—KIBLER and McBRIDE (*Jour. Infect. Dis.*, July, 1917, p. 13) found that the immediate results of the intravenous injection of typhoid vaccine, such as chill, rise and fall of temperature leukocytosis, and changes in the concentration of agglutinin and opsonin, usually in the direction of an increase, were the same in the normal man as in the typhoid patient, and the results

do not support the view that the reaction is essentially specific. Except insofar as the results show that leukocytosis is rather constant after the injection of vaccine they do not appear to support any particular view advanced to explain the action of intravenous injection of foreign protein in infectious diseases. The number of cases observed by us is too small to allow any conclusions as to the therapeutic effect of typhoid vaccine in typhoid fever, but the results obtained would seem to correspond fairly well with the results obtained in larger series.

Plea for Greater Care in the Performance of Duty by Medical Officers at Recruiting Stations.—FARENHOLT (*U. S. Naval Medical Bull.*, July, 1917, p. 318) states that the examiner should regard his duties most seriously, should strive to develop a nicer sense of observation, remembering that a compromise with established physical standards can only result disastrously, and he should adopt for the examining room the motto, "Quality, not quantity."

The Etiology of Common Colds.—FOSTER (*Jour. Infect. Dis.*, November, 1917, p. 451) concludes from his experiments that the following facts have been established: Common colds of the ordinary type are infectious. The ordinary bacteriological methods that have been resorted to heretofore do not furnish reliable criteria on which to base conclusions as to the etiology of these affections. Cultures made from the nasal secretions early in the acute phase often remain sterile, while cultures made later in the attack frequently show such a diversity of organisms that only presumptive evidence exists for ascribing to anyone an etiological role. It has been demonstrated experimentally that the virus of common colds occurs in the nasal secretions and that this virus is capable of passing through Berkefeld filters, which are impermeable to ordinary bacteria. By the employment of special anaërobic methods the virus of common colds has been cultivated *in vitro* and has proved capable of repeated recultivation in subcultures. Experimental inoculations have demonstrated that Berkefeld N filtrates of subcultures of the virus, in the second generation at least, are infective. A peculiar minute microorganism has been isolated from cultures made from the filtered nasal secretions in common colds. This microorganism can be passed through Berkefeld N filters and has been recultivated from culture filtrates. Although conclusive proof of its nature has not been adduced the experiments suggest that the microorganism described bears a definite relation to the true infective agent.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PETERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A

Alcresta Tablets of Ipecac

Enable You to Give Large Doses of Ipecac
Without Nausea



USEFUL when you wish to administer Ipecac in Chronic Tonsillitis, Acute Bronchitis, Bronchial Asthma, Intestinal Stasis and Enteric Infections.

Each tablet represents the full therapeutic activity of ten grains of Ipecac, U. S. P.—uncoated—disintegrating—non-nauseating.

Alcresta Tablets of Ipecac are supplied through the drug trade in bottles of 40 and 500.

SEND FOR FURTHER INFORMATION

HEMAGULEN—

a Hemostatic Prepared from Fresh
Brain Substance

INDICATED in hemorrhage after the removal of adenoids and tonsils and other operations on the nose and throat and in all persistent hemorrhages from small vessels where it can be applied to the bleeding surface. Physicians and dentists are using Hemagulen with fine results.

*Supplied Through the Drug Trade in
Ounce Bottles*

Send for Literature on Hemagulen



MADE ONLY BY

ELI LILLY & COMPANY, Indianapolis, U. S. A.

New York

Chicago

St. Louis

Kansas City

New Orleans

Pluriglandular Insufficiency

"THE practitioner should grasp the idea that morbid states may be consequent upon pluriglandular insufficiency and this will encourage him to substitute multiglandular for monoglandular organotherapy on the same lines and for the same reasons that we employ polyvalent sera." Dardel: "The Practitioner," July, 1912.

Hormotone

is a pluriglandular preparation that has met with the approval of many leading clinicians. It is prepared in two forms, Hormotone and Hormotone without Post-Pituitary.

Hormotone is used for all conditions dependent upon adrenal insufficiency, as evidenced by asthenia, sensitiveness to cold and cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation and psychasthenia.

A well known American physician writes: "No medicine of this character has ever been devised that produces the uniformly good results that Hormotone does when used in suitable cases."

In neurasthenia associated with high blood-pressure and all hypertensive conditions use

Hormotone without Post-pituitary

This preparation was mentioned very favorably by a writer in "The Practitioner" for November, 1917. (See page 481.) Dose of either preparation: One or two tablets three times daily before meals.

LITERATURE UPON REQUEST

G. W. CARRICK COMPANY

13 Sullivan Street

New York



DOCTOR, Have You Patients Convalescing from Spanish Influenza or Pneumonia?

And are you puzzling your head this very moment for the right place to send them?

—where they will find the badly needed change of air and scene in a thoroughly delightful climate.

—where they will be assured of purest water and proper food, supplemented, if necessary, by special treatments.

—where they will be surrounded with opportunities for healthful diversion and recreation.

—and where there is no long, hard and incidently expensive journey to tax their strength.

There is just such a place. With all these advantages. It is—

OLD POINT COMFORT, VIRGINIA

Hotel Chamberlin

At the Greatest Center of Military, Naval and Aërial Activity in America. Delightful walks and drives. Dancing, Golf, Tennis, Sea Bathing every day of the year. A complete Electro-Hydro-therapeutic outfit. Sea Foods, Southern Cookery.

For further or any special information, write our Resident Medical Director.

DR. SAMUEL G. TRACY

Hotel Chamberlin

Fortress Monroe, Va.

*For Hotel Rates, Reservations, etc., address
Geo. F. Adams, Manager, Fortress Monroe, Va.*

CONTENTS

ORIGINAL ARTICLES

- The Early Diagnosis of Lead Poisoning, with Special Reference to Abdominal Pain** 781
By GEORGE L. APFELBACH, A.B., M.D., Chicago, Ill.
- The Opaque Meal Versus the Stomach Tube in the Diagnosis of Gastric Hypomotility** 795
By I. H. LEVY, M.D., Professor of Medicine, Syracuse University, Syracuse, N. Y.
- Aplastic Anemia** 799
By J. P. SCHNEIDER, M.D., Assistant Professor of Medicine, University of Minnesota Medical School.
- The Diagnosis and Treatment of Diaphragmatic Pleurisy: with Report of Cases** 808
By T. H. KELLY, B.S., M.D., Instructor in Medicine, University of Cincinnati; Assistant Attending Physician, Cincinnati General Hospital, and H. B. WEISS, A.B., M.D., Instructor in Medicine, University of Cincinnati; Assistant Attending Physician, Cincinnati General Hospital; Physician in Charge, Wilhelm and Gette Beckman Dispensary, Cincinnati, Ohio.
- The Fractional Examination of the Duodenal Contents** 817
By MAX EINHORN, M.D., Professor of Medicine at the New York Postgraduate Medical School, New York.
- Certain Aspects of the Clinical Value of the Estimation of Kidney Function** 830
By EDWARD H. MASON, M.D., Montreal, Canada.

(Contents continued on page 6)

AS AN AID IN DIAGNOSIS

Use a Laboratory Whose Personnel and Equipment Are Beyond Question
Accuracy, Dependability and Promptness are Our Chief Aims

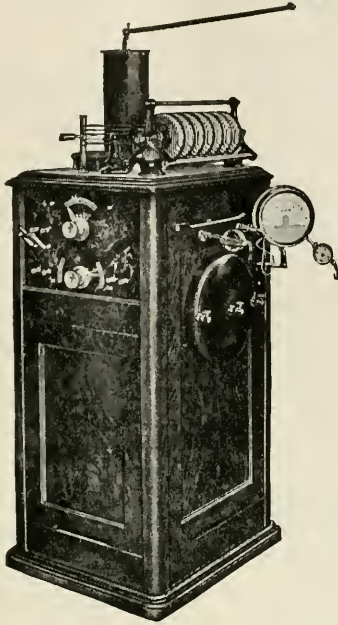
Send to our nearest laboratory for fee list and containers with instructions for collecting all specimens. ∴ These containers will be sent gratis upon request

NATIONAL PATHOLOGICAL LABORATORIES (Incorporated)

CHICAGO
5 South Wabash Avenue

ST. LOUIS
4485 Olive Street

NEW YORK
18 East Forty-first Street



Keeping In Step With Progress

THE increasing use of high frequency currents, both in medicine and in surgery, has been responsible for the design of an apparatus which would be more commensurate with the requirements of today, and it is with a great deal of pleasure that we introduce

*The newest member of the
"Victor Family"*

Model Wantz High Frequency Apparatus

HERE ARE SOME OF THE OUTSTANDING FEATURES:

A new and original design of spark gap and regulator—the first one that we or anyone else could honestly claim will stand up under hard, continuous service, is practically noiseless in operation, self-cooling, and is practically self-cleaning.

An oil immersed transformer—another innovation which puts this apparatus on the same footing with the best interrupterless transformer construction of today.

Two outfits in one cabinet—both Tesla and d'Arsonval windings are incorporated into this single apparatus, which gives the operator complete range of all high frequency modalities, including both Tesla and d'Arsonval auto-condensation

currents, in addition to refined and smooth currents for diathermy, fulguration (both hot and cold spark), inhalation, vacuum electrode, etc.

Increased flexibility and refinement of control—each and every modality is available with the widest possible current range, (even in excess of present day requirements) and a greater refinement of control than has been heretofore available from any type of high frequency apparatus.

A number of other good features (some of which are exclusive) are described in the new bulletin, together with detailed illustrations, which is now ready for distribution. Send for your copy today. No obligations.

VICTOR ELECTRIC CORPORATION

Manufacturers of Roentgen, Electro-Medical and Physical Therapeutic Apparatus

CHICAGO
236 S. Robey St.

CAMBRIDGE, MASS.
66 Broadway

NEW YORK
131 E. 23rd St.

Sales and Service Stations:

NEW YORK
131 E. 23rd St.
CAMBRIDGE
66 Broadway
CHICAGO
236 S. Robey St.
30 E. Randolph St.
PHILADELPHIA
25 S. 17th St.
OMAHA
390 Brandeis Theatre Bldg.
DENVER
1415 Glenarm St.
SEATTLE
52 Cobb Bldg.
PORTLAND, ORE.
553 Pittock Bldg.
KANSAS CITY, MO.
414 E. 10th St.

ALBANY, N. Y.
82 S. Grove Ave.
OKLAHOMA CITY
1610 N. College Ave.
LOUISVILLE
433 Atherton Bldg.
ROCHESTER, N. Y.
840 Genesee St.
NEW ORLEANS
606-608 Malson Blanche
LOS ANGELES
4002 Walton Ave.
MINNEAPOLIS
220 La Salle Bldg.
HOUSTON
901 Willard St.
AUSTIN, TEX.
708 Colorado St.

CLEVELAND
505 Frederick Bldg.
PITTSBURGH
620 Fulton Bldg.
FT. WAYNE, IND.
1333 Cathoun St.
DES MOINES
518-22 Utica Bldg.
WINNIPEG
Keewayden Block
VANCOUVER
808 Richards St.
SAN FRANCISCO
334 Sutter St.
BUFFALO, N. Y.
318 Pearl St.
ATLANTA
513 Hurt Bldg.

WAR MEDICINE

Open Pneumothorax: Its Relation to the Treatment of Empyema 839
 By MAJOR EVARTS A. GRAHAM, M.C., and CAPTAIN RICHARD D. BELL, M.C., of the Empyema Commission, United States Army.

Irritable Heart or Effort Syndrome 872
 By CAPTAIN THAYER A. SMITH, M.C., Cardiovascular Specialist, and MAJOR DAVID BOVAIRD, M.C., Chief of Medical Service, Camp Dix, New Jersey.

Clinical Report upon Cases of Lobar Pneumonia Treated with Antipneumococcus Serum as Observed at General Hospital No. 6, Fort McPherson, Georgia, October, 1917, to May, 1918 887
 By LIEUT.-COLONEL C. N. B. CAMAC, M.C., U.S.A., New York.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE

W. S. THAYER, M.D., ROGER S. MORRIS, M.D.,

AND

THOMAS ORDWAY, M.D.

Clinical Significance of the Abnormally Wide Ventricular Deviation in the Electrocardiogram 894

Studies on Renal Function during and Immediately Following Some of the Acute Infectious Diseases 894

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

Pleural Infection in Wounds of the Chest; Pleurectomy for Old Suppuration with Pachypleuritis 895

Mixed Tumors of the Salivary Glands 896

(Contents continued on page 8)

CLINICAL LABORATORY ANALYSES	DEPARTMENTS for SEROLOGY, CHEMISTRY, PATHOLOGY BACTERIOLOGY, SANITATION
	ABSOLUTELY ACCURATE TECHNIQUE
LABORATORY OF PATHOLOGY AND BACTERIOLOGY 1130 Marshall Field Annex Building, 25 East Washington Street, CHICAGO FEE TABLE AND STERILE CONTAINERS ON REQUEST	

RADIO-ACTIVE WATER

FRESH EVERY DAY

Chronic Rheumatic and Arthritic Patients

renting

Radio-Rem

usually buy the outfits at the end of the rental period. This shows that their physicians are satisfied with the radium emanation treatment. The RADIO-REM apparatus is most simple and convenient, and the rental plan makes it inexpensive.

Radio-active water should not be given as a last resort—because better results follow the treatment in earlier cases.

WRITE TO

Schieffelin & Co.

-

-

-

New York



For Influenza

AND COLDS

"Salipyrin was extensively used during the epidemic of influenza in 1891, and highly extolled for efficiency therein, as well as for its freedom from cardiac action."

(Prof. S. O. L. Potter, *Materia Medica*, page 468).

If given early in the attack it generally succeeds in aborting it altogether. In any case the drug moderates the severity and shortens the duration of the disease.

RIEDEL & Co., INC.

35 WEST THIRTY-SECOND STREET, NEW YORK

CONTENTS—(Continued)

Transfusion with Preserved Red Blood Cells	896
Abuse of Drainage Tubes	897
New Pathology of Syphilis	897
Intravenous Injections of Sodium Iodide in Massive Doses in Obstinate Syphilis	898
Gunshot Wounds of the Peripheral Nerves	898
Empyema in Base Hospitals	899

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Etiology and Treatment of Pruritus Ani	900
Treatment of Influenza Pneumonia by the Use of Convalescent Human Serum	901
Serum Treatment of Type I Pneumonia Occurring in Association with an Epidemic of Influenza	901
Rat and Poliomyelitis	902

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Cesarean Section for Eclampsia	902
Cesarean Section in Twin Pregnancy with Unusual Complication	903
Spontaneous Evolution of a Transverse Presentation	903
Mortality among Women from Causes Incidental to Childbearing	903
Cesarean Section for Contracted Pelvis, Double Uterus and Multiple Fibroids	905
Nitrous Oxide Oxygen Analgesia in Normal Labor and Obstetric Opera- tions	905
Problems of Social Order in the Interest of Mother and Child	906
Tetanus Neonatorum	907

(Contents continued on page 10)

PHILADELPHIA CLINICAL LABORATORY, Inc.

E. Q. ST. JOHN, M. D., President

PROFESSIONAL BUILDING, 1833 CHESTNUT STREET, PHILADELPHIA

GENERAL CLINICAL AND BACTERIOLOGICAL ANALYSES

Autogenous Vaccines—Wassermann's Reaction—Abderhalden's Tests
Analysis of Drinking Water and Milk

Price list and Containers mailed on request

For Intestinal Disturbances, etc.

Ichthalbin

(*Ichthyol albuminate*)

An easily absorbed preparation of Ichthyol for *internal* use
Indicated also in skin diseases and cachectic conditions

Dose: For adults, 10 to 30 grains; for children, 5 to 10 grains, three times daily
in powder or 5-grain tablets

IN DANDRUFF

LOSS OF HAIR AND DISEASES OF THE SCALP

prescribe

Euresol pro capillis

A liquid resorcin preparation, exerting a powerful antiseptic and
stimulating action on the scalp

Used in 3 to 5 per cent. lotions as hairwash, also in salves

Literature and formulas from E. BILHUBER, 45 John Street, NEW YORK

THOUGHTFUL PHYSICIANS are using the

Nicholson Princo Sphygmomanometer

The *folding pocket mercurial* instrument with the *full length* manometer tube and scale graduated in single mm.

Read what they say:

DR. CABOT—"Physical Diagnosis." Pages 107-110

DR. NORRIS—"Blood-Pressure, its Clinical Application." Page 132

DR. GOODMAN—"Blood-Pressure in Medicine and Surgery." Page 56

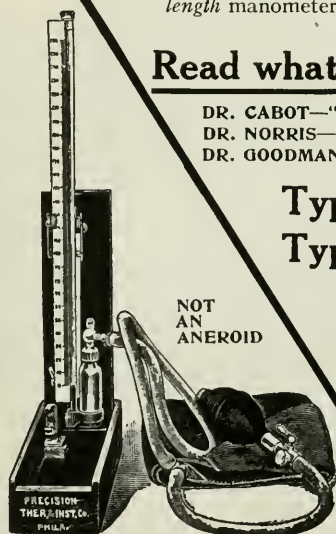
Type A, \$22.50 (260 mm)

Type B, \$24.00 (300 mm)

Our little booklet "Blood-Pressure," contains a complete description of this instrument. We'll be glad to send you a copy along with a pamphlet on the Clinical Significance of Diastolic and Pulse Pressure. Free for the asking.

Precision Thermometer & Instrument Co.

1434 Brandywine Street
PHILADELPHIA, PA.



NOT
AN
ANEROID

CONTENTS—(Continued)

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

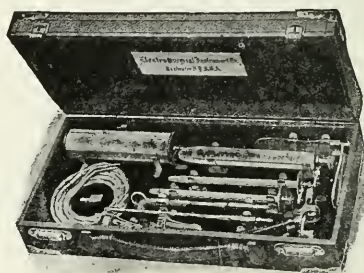
MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.

Bacteria of Gangrenous Wounds	908
Combined Preventive Inoculation against Typhoid and Paratyphoid Fever and Bacillary Dysentery	910
Methods of Destroying Lice	910
Production of Antipneumococcus Serum	911
Suggestions Concerning the Prevention and Cure of Acute Lobar Pneumonia	911
Bacteriology of the Bubble Fountain	912
Effects of Exposure to Cold upon Experimental Infection of the Respiratory Tract	913

ACCURATE DIAGNOSIS MADE POSSIBLE

Certainty

of diagnosis—accuracy of treatment—both are facilitated by the use of electrically lighted instruments, which give an actual view of the parts. E. S. I. Co. instruments are made according to the ideas of leading physicians and surgeons, as for example: **Holmes, Jackson, Tuttle, Lynch, Braasch, Koch, Swineburn and Young**, and include Nasoscopes, Proctoscopes, Sigmoidoscopes, Cystoscopes and many others. All are fitted with superior lamps. Brilliant illumination at trifling cost.



Modern General Diagnostic Outfit

This outfit now weighs but 4½ pounds, and measures 3½ x 7 x 15 inches, making it very convenient to carry.

All E. S. I. Co. instruments are warranted mechanically and electrically perfect.

*Illustrated and descriptive catalog sent on request.
Be sure of exact name.*

ELECTRO SURGICAL INSTRUMENT CO.
ROCHESTER, N. Y.



THIS IS THE SIGN

Which stands for
Combined Efficiency and Safety

in the Relief of

PAIN, INFLAMMATION and CONGESTION

By Internal Medication

No constipating, cumulative, cardiac depressant or renal irritant by effects

ATOPHAN IS MADE IN U. S. A. AND FURNISHED IN

Tablets, 7½ grains, twenty in box

Powder, in 1 ounce cartons

SCHERING & GLATZ, Inc.

150 Maiden Lane, New York

Laboratory Table



MAKES LABORATORY
WORK A PLEASURE

EVERYTHING NEEDED
WITHIN EASY REACH

*Increases Efficiency
Creates Confidence*

ASK YOUR DEALER OR
WRITE DIRECT FOR
BULLETIN No. 118

CHICAGO SURGICAL AND ELEC-
TRICAL COMPANY, Manufacturers

322 W. Superior St.
CHICAGO, ILL.



Pneumonia and Empyema

The high percentage of deaths from infection by the *streptococcus hemolyticus* complicating pneumonia, warrants our calling attention to the importance of

1st. IMMUNIZATION

Preventing Infection with an appropriate Serobacterin or Bacterin. Reports from physicians in charge of medical work connected with industrial institutions, boards of health, and general practitioners, abundantly justify the prophylactic use of Influenza Serobacterin containing the organisms isolated from the present epidemic, in preventing influenza and pneumonia.

2d. TREATMENT

In **streptococcus pneumonia** the early use of Antistreptococcic Serum Polyvalent administered intravenously, in full doses (100 to 200 mils), repeated every 8 to 12 hours or as indicated. This serum contains the antibodies against the different streptococci isolated from the present epidemic. Especial reference is made to the *streptococcus hemolyticus*.

In **pneumococcus pneumonia** the early use of Antipneumococcic Serum Polyvalent administered intravenously in full doses (100 to 200 mils), repeated every 8 to 12 hours or as indicated. The Medical Departments of the United States Army and Navy recognize the serum treatment as specific.

In **mixed infections** the conjoint use of both sera is indicated.

We prepare a **Monovalent Antipneumococcic Serum Type I** and a **Polyvalent Antipneumococcic Serum**. The polyvalent serum contains the same amount of antibodies against Type I pneumococcus as the Type I serum and in addition contains antibodies against Types II and III.

The danger of delayed administration of serum while making type determination and the danger of re-infection during convalescence is recognized; therefore, preference may be given to the **polyvalent serum** in routine practice where type determination is impractical.

These Serums are furnished in 50-mil Ampule with apparatus for intravenous injection.

Literature mailed upon request

H. K. MULFORD CO., Philadelphia, U. S. A.

Manufacturing and Biological Chemists

36553

THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

DECEMBER, 1918

ORIGINAL ARTICLES

**THE EARLY DIAGNOSIS OF LEAD POISONING, WITH SPECIAL
REFERENCE TO ABDOMINAL PAIN.**

BY GEORGE L. APFELBACH, A.B., M.D.,
CHICAGO, ILL.

WITH the advent of compensation for industrial diseases the profession will concern itself with an early diagnosis of lead poisoning in order to reduce the disability in such cases to give those afflicted their due consideration and to prevent malingering. Switzerland and Great Britain pay for lead disability as for accident, and for this reason have produced much accurate information for the early diagnosis of plumbism. Physicians in this State have become more and more critical in detecting lead poisoning, since compliance with the Occupational Disease Law gives a medicolegal advantage to the employer. We propose to lay down a definite standard for an early diagnosis.

From a purely scientific and humanitarian standpoint an early diagnosis is desirable in order to prevent the rapid fatal intoxications and also the sequelæ of lead, which Naegli calls meta-lead conditions, as nephritis, arteriosclerosis, cerebral hemorrhage and neurological conditions, such as paralysis, premature senility, neurosis and insanity.

We propose, in addition to this, to call attention not only to the differential diagnosis of lead colic but to the possibility of confusing milder abdominal pain from lead with that caused by abdominal conditions.

In order to effect our purpose we shall refer to three groups of lead examinations:

1. The Illinois Department of Factory Inspection has received reports of 1238 cases of lead poisoning from July 1, 1912, to July 1, 1917, but owing to the lack of specific information in early reports we can depend only on the last 934 case records, because they were made more in detail, since a list of common lead findings on the report blanks stimulated the examining physician to more careful observation and recording of the findings. These examinations were made with a varying degree of completeness by physicians throughout the State. Since there is a decided medicolegal advantage in reporting plumbism to the State Department, early diagnoses have been made and the symptoms and signs reported are early observations. Allowance must be made here and there for an absence of detail observation, since these factory examinations are often made in haste. Chart I refers to these reports.

2. Chart II refers to 72 cases of lead poisoning in which the examinations were made by the writer. In these the diagnosis is practically certain because basophilic degeneration, colic, lead tremor, lead anemia, usually in combination with constipation, were established. Very few of these cases were severe and were not of the type usually seen in hospital wards. They occurred in the lighter lead trades, such as painting, soldering, battery manufacturing and brass founding. For accuracy in deduction the writer is more inclined to use this smaller series than the larger number of cases reported in Chart I. Charts II, III and IV refer to the writer's own case records.

3. We further refer to Chart V, where the writer presents in tabulated form the results of 150 critical examinations of house painters not incapacitated but sent to the writer for the purpose of ascertaining early signs of plumbism and to furnish data for the improvement of health conditions in this trade. We have since that time examined 30 printers and 75 more painters.

The above series of examinations brings out some important points in the diagnosis of lead poisoning, since they differ from the stereotyped pictures found in the classical text-books of medicine. We hope that this paper will explain why Cabot found evidence of undiagnosed plumbism in many of his autopsies.

The lead symptom-complex is so variable that a description is difficult, as all this may be dependent (1) on the dosage and rapidity of dosage; (2) on the presence of alloys in the metals ingested; (3) on the fact whether the intoxication occurs in the form of fumes or in the inhalation and swallowing of lead dusts; (4) on the individual susceptibility, sex, age and personal habits.

There are about 150 different lead trades from which can be derived all forms of plumbism. Among painters and printers we

see mild forms, oftentimes escaping the attention of the physician, only later to be recognized as a meta-lead condition. The more severe forms are found in workers in lead smelters and white lead manufactories, where, without prodromata, the attack begins with a rapid emaciation, cachexia and colic. We recall one case in which the worker was seized with convulsions while feeding a Scotch hearth furnace without any previous complaint.

Recognizing that many workers are found ingesting and excreting lead without clinical findings we must acknowledge such early cases that the evidence of the condition is meager and that between this picture and the severer forms there are many degrees in the occurrence of the various findings and the duration of the symptoms. In speaking of the different forms of plumbism there is also a tendency among students of lead poisoning to recognize meta-lead conditions in which they observe nephritis, arteriosclerosis and brain and cord changes.

Discard the stereotyped pictures in your text-book and the typical hospital cases. Realize that the symptom-complex of an early lead poisoning is often devoid of many of the cardinal signs. Naegli, of Switzerland, has described this as the monosymptomatic occurrence of plumbism, and our findings support this view. In many forms there are no basophilic granules, no blue lines, no wrist-drop and even no anemia. Chart IV reveals cardinal findings of lead poisoning occurring oftentimes in early cases in twofold or threefold groups. The consensus of medical opinion points toward blue line, basophilic degeneration of the red cells, tremor, pallor and anemia, constipation and colic as cardinals. The data which we present substantiate this. However, the writer would prefer, instead of the common term of lead colic, the expression colic and abdominal pain from lead.

In the series of 934 cases, blue line, pallor and anemia, constipation and colic predominate, although blue line leads in the frequency of occurrence for reasons to be mentioned later. Constipation is the most constant finding, occurring 335 times, followed next by colic and anemia.

In the writer's series of 72 cases, constipation, pallor and anemia, colic, stippling, blue line and tremor are constantly observed: constipation in 81.9 per cent., tremor in 72.2 per cent., pallor and anemia in 65.2 per cent., basophilic degeneration in 51.3 per cent., pain in the abdomen of varying types in 56.9 per cent. and blue line in 26 per cent.

Considering the six findings just mentioned as cardinals it is interesting that they occurred altogether in 1 case, five times in 5, four times in 4, three times in 20 and two times in 14 cases. Chart III shows the variations of these cardinals.

In addition to these the lead-worker complains of pains in the

back, limbs and joints, probably ascribable to neuritis. This was found distinctly true in 13 cases, including 1 sciatica. Among 150 painters, 35 complained of lumbago, 42 of pains in the right shoulder, 50 of joint pains and 20 of neuralgias. The neuritis in early cases seems to affect the part most used, as, for instance, the shoulder when working with a heavy brush and the wrist when doing fine work. Strange to say we find with the hand dynamometer a paradoxical diminution in the strength of the hand most used.

Before proceeding with a discussion of the cardinals we again emphasize that plumbism is variable and that often not all the cardinal findings are in evidence.

CONSTIPATION. Constipation occurs early in the lead-worker and is quite a constant finding in this disease. Its occurrence of from 80 to 90 per cent. is to be noted in European reports as well as in the statistics of this paper. The low percentage among the factory reports occurred because many workers with blue lines were reported as lead cases when no other clinical evidence could be found, but they were inserted in the report to safeguard the employer. Among 150 painters there were 24 mild complaints of constipation, 39 moderate and 10 severe, a total of 73, or 40.1 per cent.

In severe intoxications the constipation becomes so marked that it resembles an intestinal obstruction.

ABDOMINAL PAIN AND COLIC FROM LEAD. In the experience of the writer more lead-workers suffer from gastric disturbances and abdominal pain than from colic. Digestive disturbances are often prodromata to the colic. The writer recalls several painters who when they work in white lead for three or four days feel a "gnawing in the stomach," gastric disturbance, for many weeks before an actual colic occurs. The State series does not give an accurate distinction between abdominal pain and colic. In the writer's series colic occurs in 31.9 per cent. of the cases, abdominal pain in 25 per cent., a total of 56.9 per cent. In the examination of 150 house painters 46 were found with some form of abdominal pain, with digestive disturbances. These men were remarkably temperate in their habits and furnished an intelligent history. The abdominal pains and digestive disturbances are very easily confused with a chronic appendicitis, a duodenal ulcer, gall-bladder disease and other abdominal conditions. Roentgenograms in lead conditions seem to produce no pathological picture, and this serves, in a measure, to differentiate from the conditions just mentioned above.

The colic itself occurs usually as a severe abdominal paroxysm, the pain, cutting and sharp in character, crossing the abdomen from side to side, usually about from two to three finger-breadths above the umbilicus. Little mention is made of lead colic in most works on acute abdomen, and since this colic, with its intense character,

is likely to occur in any part of the abdomen, oftentimes bringing up the question of surgical interference, the writer has compiled a series of 23 cases of lead colic in which the diagnosis might suggest acute abdomen. In many of these cases the colic occurs not only about and around the umbilicus but also in the region of the bladder and of the appendix, and even resembles a renal colic. Woodard, United States Navy, in 1913, demonstrated 3 cases of typical appendix history, with a slight rigidity and tenderness over McBurney's point, which later proved to be cases of lead poisoning; 2 of them were unfortunately operated.

The colic is usually relieved by pressure or by flexing the thighs, and seems to be much out of proportion to the actual tenderness. Naegli differentiates malingering from lead colic by this fact. If in pressing or palpating the abdomen the patient cries out he decides it is not lead poisoning unless he feels assured that he is dealing with a hysteria or a marked neurasthenia. He then tells such patient that lead colic never produces such tenderness, whereupon the malingerer ceases his outcries. The writer, however, would make an exception in that type of colic which is accompanied by abdominal distention in which upon pressure tenderness and distress occur.

. During the attack of the colic we notice a diminished urine, oftentimes a slow pulse, pallor, cold, clammy sweats and in about one-half of the cases vomiting.

Since lead colic is rather a common condition and may appear in any region of the abdomen, in the diagnosis of an abdominal pain not only should the hand be put under the sheets to palpate the abdomen, but in all cases should a most thorough physical examination be made from head to toes. This would not only reveal lead colic, but would, I believe, often lead to discovery of tabes, pneumonia, Pott's disease and other elusive conditions. The writer has studied the lead colic question from two standpoints—namely, the industrial and surgical—and has found in his experience that a lead colic most often resembles an acute gastritis, a gall-bladder, an appendix, the gastric crisis of tabes, angina sclerotica abdominalis and an intestinal obstruction. Reference to any standard work on the causes of abdominal pain or acute abdomen will enumerate the numerous other conditions that might be mistaken for lead colic.

It is a deplorable habit of some medical men to jump at the conclusion of lead poisoning and colic when their patient happens to be a painter or lead-worker. There is no reason why a lead-worker should not become sick with a diverticulitis, appendicitis or a Dietl's crisis. The lead-worker is also prone to attribute every abdominal pain to his trade. The writer was once called in consultation when a physician diagnosed the case as acute appendicitis, but the family had some doubt about it because the patient was a

painter. The patient had had lead colic on several previous occasions, but this time the diagnosis proved to be an appendix, marked by tenderness, rigidity, temperature and leukocytosis, and was so confirmed by the operation.

TREMOR. Tremor is often a neglected sign of lead poisoning, being very evident in the severer forms and not observed in the incipient type. With proper limitations this sign can often determine the diagnosis when stippling and blue line are absent. In the series in Chart I tremor was reported in 14.45 per cent. of the cases. Naegli found it eighty times in 140 mild cases; the writer found a fine finger tremor in 18.1 per cent. and a fine tongue tremor in 72.3 per cent.

The tremor in lead poisoning is especially fine in character, having about the same rapid vibration as the tremor of hyperthyroidism. It is fine and more rapid than the usual tremor seen in neurasthenia, nicotin and other drug conditions, and yet might be confused with these. An alcoholic tongue or finger tremor should not be confounded with a lead tremor, the former being coarse and the latter fine. The writer has seen a simultaneous lead and alcohol tremor in alcoholics, the former assuming a fibrillary twitching, especially seen along the lateral margins of the tongue.

The fact that the fine lead tremor cannot be simulated makes it a valuable sign not only for a differential diagnosis but also for detecting malingering. The tremor is a sign which appears early in many lead-workers and can be observed long before the occurrence of a colic or before the lead-worker becomes conscious of illness. Its occurrence should warn against an impending attack. Out of 150 painters a fine tremor was noticed on the tongue or on the fingers 56 times and a coarse tremor 40 times.

The tremor disappears slowly, often lasting for months. For this reason one ought to inquire carefully whether the tremor on its detection antedates the colic or is a sequel of it.

PALLOR AND ANEMIA. Anemia is an early sign and is usually associated with pallor, the latter being out of proportion to the actual hemoglobin estimate. The Tallquist is a valuable instrument in a lead plant. The reduction of hemoglobin in the course of monthly examinations should not be disregarded. The anemia is due to the destruction of blood cells both in the vessels and in the marrow.

An interesting article by Byfield, recently published in the *Illinois State Journal*, refers to the occurrence of pernicious anemia in the printing trade and clearly points out the effect of lead on the blood and on the blood-forming organs. In his experience the writer has seen the occurrence of five or six primary anemias in the printing trade and is at a loss to determine the cause, being in doubt whether it be a coincidence, whether it be due to lead or whether this anemia

be the result of benzol, a substance which also destroys red and white blood cells and is used in this trade. Before forming definite conclusions we feel that the matter should be more thoroughly investigated.

BLUE LINE. Much has been written on the blue line. The deposit of lead sulphide on the margin of the gums occurs only when there are teeth and when they are ill-kept. The line has a grayish-black tinge, the surrounding gum being somewhat bluish, as in Chadwick's sign of pregnancy. When there is doubt as to the existence of the blue line, Charles Spencer Williamson has advised the use of a hand lens. The occurrence of a blue line on the gums indicates metallic absorption and does not always indicate the use of lead, nor does this blue line indicate illness or disability, nor does its absence prohibit the diagnosis of lead poisoning. In the writer's series of 72 cases the lead line was observed in only 36.1 per cent.

Lead not only produces this characteristic phenomena on the gums but seems to destroy the teeth so that one will see lead-workers more often with decayed teeth and pyorrhea than with a lead line. In 150 painters a blue line was observed only 5 times, loose teeth 32, decayed teeth 52 and pyorrhea 32 times; only 11 painters were observed with good teeth. This condition is not seen in other trades of the same nationalities, habits and house and living conditions.

Grawitz thought that he had established the fact that all lead cases showed punctated reds; Naegli, however, found in 112 mild cases out of 169 colics 34 without stippled cells. These basophilic granules are seen in some normal persons, in cachexia, tuberculosis and malaria, but never in such large numbers as in plumbism. They are supposedly due to a regenerative or a degenerative process in the red cell.

Out of 50 preparations made from painters the writer found stippled cells in 12; in 72 cases reported stippling was found 37 times, or 51.3 per cent. Paul Naegli and Schnitter hold that with improved staining methods basophilic granules can be found in nearly all chronic cases of plumbism.

Naegli and Schnitter recommend the use of a methylene-blue stain. We also found greater success in the use of a Wright than of a Skelton or Giemsa stain.

To make a diagnosis of lead poisoning, Paul Schmidt states there should be 100 stippled cells out of 1,000,000 reds. Naegli insists upon counting for ten minutes before he dismisses the preparation as negative. These methods are both commendable for their accuracy. We feel that when average technic is used in examining a preparation a stippled red should be found in ten minutes, and that if none is observed the result is called negative.

Other blood findings in lead poisoning are chromatophiles in severe forms, macrocytes, microcytes and stippled normoblasts. Schnitter states that if the compensatory power of the blood-forming organs disappears, basophilic cells disappear.

Leukocytosis has been referred to as a blood finding, giving the average number of cells between 8000 and 10,000, hence a marked increase of the white cells is rare.

SUBSIDIARY FINDINGS. To finish our picture, reference must be made to some of the other findings in lead poisoning, as, for instance, rapid emaciation, loss of muscular strength, headaches, loss of vision, scaphoid abdomen, slow pulse, strangury, arthritis, lead paralysis of various forms, severe trembling, lead encephalopathy, anaesthesia and hyperaesthesia and reflex disturbances.

One word more in regard to blood-pressure which does not appear to be consistently present during an acute attack. When blood-pressure has been reported in the State reports as a high-tension pulse there may have been other factors. At least we have never observed this sign as a usual finding. The systolic blood-pressure in the examination of 150 painters was, on an average, 132 for men between 20 and 29 inclusive; 132 between 30 to 39; 143 between 40 and 49; 150 between 50 and 59; 187.5 between 60 and 69; 210 over 70. The rise in blood-pressure from lead is more liable to be a result of meta-lead condition than an actual finding during the manifestations of an acute or subacute attack.

CONCLUSIONS. From the data on hand collected and studied by the writer we present the following conclusions:

1. The manifestations of an intoxication with lead are variable, sometimes presenting only one or two of the cardinal signs of this intoxication, which are colic, constipation, blue line, tremor, basophilic degeneration of the red cells and pallor and anemia.

2. An early diagnosis of plumbism can be established by the history of lead working, by the presence of constipation, plus one or more of the cardinals: fine tremor, blue line and basophilic degeneration of the red cells. Constipation with pallor and anemia or with colic presents a suspicious picture which must be worked out by the aid of subsidiary findings.

3. Anemia and fine tremor are very early signs of plumbism.

4. As more lead-workers suffer from vague abdominal pains and gastric disturbances than from colic the differential diagnosis of any abdominal pain or colic or digestive disturbance demands the consideration of lead as the possible cause.

5. There does not seem to be a consistent rise in blood-pressure in acute or subacute cases of lead poisoning.

6. Over one-third of house painters show signs of plumbism. The high incidence of nephritis, arterial disease and pulmonary tuberculosis in this occupation must also be emphasized.

CHART I.

Out of 934 cases of lead poisoning we enumerate the findings in the number of times reported.

		Per cent.
Blue line	518	55.4
Anemia	341	36.5
Constipation	335	35.87
Colic	295	31.58
Pallor	244	25.48
Coated tongue	215	21.3
Loss of muscular strength	161	17.1
Tremor	135	14.45
Abdominal tenderness	131	14.0
Slow pulse	130	14.0
Nausea	113	12.1
High-tension pulse	74	7.9
Headache	74	7.9
Loss in weight	50	5.3
Albuminuria	27	2.88
Dyspepsia	26	2.8
Wrist-drop	24	2.57
Abdominal pain	18	1.9
Other paralyses	10	1.0
Vertigo	11	1.0

Other symptoms reported were muscular pains, neuritis, sciatica, dermatitis, diarrheas, anorexia, visual disturbances, alopecia, conjunctivitis, ulcerations, rapid pulse, eructations, lumbago, metallic taste, jaundice, cyanosis, speech disturbance, ataxia, tinnitus and epileptiform seizures.

The result of blood smears were reported but not in sufficient number to warrant tabulation.

CHART II.

In a critical examination of 72 cases of lead poisoning the following symptoms and signs occurred the following number of times:

		Per cent.
Constipation	59	81.9
Stippling	37	51.3
Blue line	26	36.1
Fine tongue tremor	39	54.1
Fine finger tremor	13	18.1
Anemia and pallor	25	34.7
Pallor	8	11.1
Anemia	14	19.4
Colic	23	31.9
Abdominal pain	18	25.0
Diminished strength in hand	7	10.0
Loss of muscular strength	7	10.0
Neuritis	12	18.0
Sciatica	1	1.4
Albuminuria	2	2.8
Convulsions	1	1.4
Cerebral hemorrhage	1	1.4
High blood-pressure	1	1.4
Coated tongue	Uncertain	

CHART III.

Considering colic, constipation, tremor, anemia, blue line and stippling as the most common findings in lead poisoning they were observed in the following combinations:

Constipation, tremor, anemia	8
Tremor, stippling, constipation	7
Tremor, constipation	6
Constipation, blue line	5
Tremor, stippling	4
Anemia, constipation	4
Anemia, constipation, stippling	4
Anemia, constipation, tremor, stippling	4
Colic, constipation, tremor, anemia	3
Blue line, stippling, constipation, colic, anemia	3
Anemia, constipation, stippling	3
Colic, blue line, tremor, anemia	2
Blue line, pallor, anemia, tremor, constipation, stippling	2
Colic, constipation, tremor, anemia, blue line	2
Colic, constipation, tremor, blue line	2
Colic, constipation, blue line	2
Constipation, stippling	2
Blue line, tremor	1
Constipation, blue line, colic, tremor, stippling	1
Constipation, anemia, wrist-drop	1
Constipation, blue line, tremor, pallor, stippling	1
Anemia, stippling	1
Colic, constipation, tremor, anemia, blue line, stippling	1
Colic, constipation, tremor	1
Colic, constipation	1
Tremor, anemia, stippling	1
Constipation, stippling, colic	1
Constipation, blue line, anemia	1
Anemia, blue line	1
Tremor, anemia, blue line	1

CHART IV.

Reference to Chart III shows that the cardinal findings of lead poisoning do not appear in all cases. The following is a short tabulation of the number of times out of 72 cases in which the cardinals appeared:

All six (colic, constipation, pallor and anemia, blue line, stippling and tremor)	1
All five cardinals	5
All four cardinals	4
All three cardinals	10
All two cardinals	9

This arrangement seems to point to the fact that in early cases of lead poisoning there is more apt to be present but a few of the distinctly cardinal signs.

CHART V.

EXAMINATION OF 150 HOUSE PAINTERS—PRESENT COMPLAINTS.

	Mild.	Moderate.	Severe.
Loss of weight	18	8	5
Loss of strength	17	10	2
Nervousness	30	11	2
Malaise	5	5	2
Pulmonary—			
Cough	23	16	
Sputum	7	3	
Hemoptysis	5	3	
Night-sweats	9	6	1
Pains in chest	32	14	3
Hoarseness	2	
Dyspnea	6	9	5
Digestive—			
Nausea	13	3	
Vomiting	4	4	2
Eructations	4	4	1
Anorexia	19	8	5
Foul taste (mornings)	12	4	
Salivary disturbances	2		
Constipation	24	39	10
Diarrhea	5	1	
Melena	1		
Hemorrhoids	6	7	2
Pain in abdomen	20	25	1
Distention	6	11	
Bulimia	1
Polydipsia	3
Sensorial—			
Headache	19	20	6
Vertigo	25	10	3
Syncope	2	..	1
Spots before the eyes	25	18	1
Tightness in chest	2	2
Nightmare	2		
Insomnia	11	7	
Rushing of blood to head	1	
Loss of memory	21	21	1
Depression	1		
Confusion	2	..	1
Diminished vision	19	19	3
Diminished hearing	5	5	1
Neuromuscular—			
Neuralgias	18	2	
Joint pains	22	28	9
Pain in right shoulder	17	15	11
Anesthesiæ	1		
Paresthesiæ	2	4	
Lumbago	25	10	2
Swollen feet	2	1
Muscular cramps	9	4	
Trembling	3	1	
Formication	1		
Diminished strength in hands (loss of hands)	1	9	
Genito-urinary—			
Night urination	9	9	5
Incontinence	1	
Impotence	1	7	3
Hematuria	1	
Stricture	1		
Polyuria	2	

CHART V.—*Continued.*

General—	Mild.	Moderate.	Severe.
Festering cuts	1		
Itching eyes	17	7	1
Lacrimation	1	..	1
Tinnitus	2	2	
Heart palpitation	2	2	

PHYSICAL FINDINGS.

Appearance unhealthy			19
Pallor			26 ¹
Emaciation			14
Adipose			13
Physical			8
Icteric			2
Prematurely aged			14
Loss of expression			5
Nephritic appearance			4
Scars on scalp			2
Tortuous temporals (marked)			5
Marked varicosities on face			6
Edema of the lids			2
Scleral hemorrhage			1
Dilated pupils			3
Conjunctivitis (mild except one)			11
Strabismus			1
Unequal pupils			4
Sluggish pupillary reflex			2
Argyll Robertson			3
Myopic (just by observation)			8
Corneal scar			1
Blepharospasm			1
Exophthalmos			2
Good teeth			11
Loose teeth			32
Decayed teeth with tartar, etc.			52
Pyorrhœa			32
Coated tongue			19
Tongue tremor—			
Fine			56
Coarse			40
Arcus senilis			10
Laryngitis			9 ²
Bad tonsils			5 ²
Diminished hearing—			
Right ear			9
Left ear			11
Bifid uvula			1
Blue line on gums			5 ³
Foul breath			5 ²
Cervical adenopathy			12 ⁴
Thyroid enlargement marked			22
Thorax—			
Pulmonary findings—			
Deformities of chest			4 ⁵
Scoliosis			4
Abnormal dullness—			
Right apex			24 ⁶
Left apex			21 ⁶
Right posterior			12 ⁶
Left posterior			9

CLASS V.—Continued.

Thorax—	
Pulmonary findings—	
Roughened respiration in apices	15
Abnormal bronchial breathing over all lungs	22
Rales in right apex	187
Rales in left apex	217
Rales under axillæ	127
Friction rubs	8
Cavities diagnosed	2
Heart findings—	
Hypertrophy left or right or both	49 ^s
Accentuated aortic second	35
Mitral murmur systolic	7
Mitral murmur presystolic	1
Tricuspid systolic	3
Aortic diastolic	4
Rough first mitral	1
Pleuropericardial rub	1
Pulse—	
Tachycardia	10
Bradycardia	2
Irregular	2
Cyanosis	7
Marked evidence of arteriosclerosis	5
Abdomen—	
Epigastric tenderness	7
Appendicular tenderness	2
Gall-bladder tenderness	2
Liver enlargement	7
Right inguinal hernia	7
Left inguinal hernia	4
Bilateral inguinal hernia	3
Epigastric hernia	1 ⁹
Umbilical hernia	1 ⁹
Femoral hernia	1
Operation scars	5
Varicocele	1 ¹⁰
Scars uncertain	1 ¹¹
Urethral stricture	2 ¹²
With active gonorrhœa	4
Phimosis	4
Hydrocele	1
Hypospadias	1
One testicle	1 ¹³
General adenopathy	3
Skin—	
Anasarca	3
Dryness	14
Dermatitis	5 ¹⁴
Eczema	2
Aene	6
Ichthyosis	1
Dermographia	1 ²
Gouty toe-joint	2
Edema ankles	6
Varicose veins	29
Syphilitic ulcer of leg	1
Varicose ulcer	1
Epitrochlear glands	3
Swollen right knee	2
Paralysis (peripheral neuritis) in arm	1
Sign of injury	1
Flat-foot marked	1 ¹⁵
Clubbed nails marked	9
Tremor in hands	6

CLASS V.—*Continued.*

Patellar reflexes—	
Unequal	5
Exaggerated	26
Absent	3
Sluggish	2
Loss of orientation	1
Loss of expression	5
Subnormal mentality	1
General spasticity	1
Urine—	
Albumin	9
Sugar	4
Casts	16
Basophilic degenerated red cells	1
Hemoglobin estimate—	
100 per cent.	22
90-99 per cent.	64
85-89 per cent.	19
80-84 per cent.	29
70-79 per cent.	3

SYSTOLIC BLOOD-PRESSURE.

Systolic blood-pressure, average—	
20 to 29 inclusive	132
30 to 39 inclusive	132
40 to 49 inclusive	143
50 to 59 inclusive	150
60 to 69 inclusive	187.5
70 and over	210

POSITIVE DIAGNOSIS MADE.

Pulmonary tuberculosis (active)	26
Incipient or latent pulmonary tuberculosis	10
Chronic interstitial nephritis	15
Heart leakage ¹	9
Diabetes	3
Exophthalmic goitre	1
Chronic nephritis	7
Epithelioma	1
Lead poisoning	3 ¹⁶
Tabes dorsalis	2

¹ Extreme in 3.² Marked.³ Marked in 2, suspicious in 3.⁴ One very marked TB gland.⁵ One from injury the others from faulty breathing and rickets.⁶ Times.⁷ Ten in both apices, 26 cases of active TB.⁸ Dilated in 7.⁹ In same individual¹⁰ Complained of, others not perhaps noted¹¹ Noticed from bubo.¹² Noted because of complaint.¹³ Removed because of TB epididymitis.¹⁴ Chiefly hands, then legs.¹⁵ Many not looked for.¹⁶ Lead intoxication diagnosed, on the basis of chronic constipation, fine tongue tremor and anemia; constipation 73, fine tongue tremor 56, anemia 51. This makes an estimate that from 51 to 73 out of 150 men show signs of plumbism in marked cases.

BIBLIOGRAPHY.

1. Naegli: Beiträge zur Kenntnis der Bleivergiftung mit besonderer Berücksichtigung des Wertes der Symptome, *Cor.-Blat. f. Schweiz-Aerzte-Basel*, 1913, xliii, 1483-98.
2. Lehman: Zur Frühdiagnose der Bleivergiftung, *Zentralblatt f. Gewerbehygiene*, April, 1913, January, 1915.
3. Weyl, Theo.: *Handbuch der Arbeiterkrankheiten*.
4. Hahn: Die Bleivergiftung in Buchdruckerigewerbe und ihre Prophylaxe, *Tr. Internat. Cong. Med.*, 1913, London, 1914.
5. Schnitter: Beiträge zur Pathologie des Blutes bei chronische bei Bleivergiftung, *Deutsch. Arch. f. klin. Med.*, Leipzig, 1915, c, xiii, 127, 154.
6. Ders: Ueber den diagnostischenwert der Blutuntersuchung bei Bleivergiftung, *Deutsch. med. Wehnschr.*, 1909, 46.
7. Williamson, Chas. S.: Finding the Lead Line with a Hand Lens, *Med. Clin. Chicago*, 1915, 414, 423, 428.
8. Ophuls: Chronic Lead Poisoning in Guinea-pigs, with Special Reference to Nephritis, Cirrhosis and Polyserositis, *AM. JOUR. MED. SC.*, Philadelphia, 1915, lx, 518-541.
9. Erlenmeyer: Experimentelle Studien über den Mechanismus der chronischen Bleivergiftung, *Verhand. d. deutsch. Kong. innere. Med.*, Wiesbaden, 1913, xxx, 455-59.
10. Anders: An Interesting Case of Chronic Lead Poisoning, with Relapse Following Fresh Exposure, *Jour. Am. Med. Assn.*, Chicago, 1914, lxii, 1164.
11. Weller: The Blastophthoric Effect of Chronic Lead Poisoning, *Jour. Med. Research*, Boston, 1915, xxxiii, 278-293.
12. Woodward: Three Cases Demonstrating the Need for Care in Diagnosis of Lead Poisoning and Appendicitis, *United States Navy Med. Bull.*, Washington, 1913, vii, 109.
13. Deaver, J. B.: Differentiation of Acute Abdomen, *Bull. Med. and Chir. Fac.*, Maryland, April, 1917, ix, 147.
14. Lancer, T. F.: The Acute Surgical Abdomen, *Med. Rec.*, 1916, lxxxix, 648.
15. Elder: The Acute Abdomen, A Clinical Study, *Canada Northern Assn. Jour.*, Toronto, 1915, v, 85-92.
16. Davis, J. D. S.: Diagnosis of Disease of Right Upper Quadrant of Abdomen, Value of Pain, Jaundice and Tumor Mass, *Am. Jour. Obst.*, lxxv, 124.
17. Eisendrath: The Acute Abdomen in Children, *Illinois Med. Jour.*, Chicago, 1915, xvii, 273-277.
18. Byfield, Arthur: Chronic Lead Poisoning in the Etiology of Pernicious Anemia, *Illinois Med. Jour.*, xxxiii, No. 2, p. 104.
19. Rundlett: Some Practical Considerations in the Diagnosis of Abdominal Conditions, *Journal-Lancet*, Minneapolis, 1915, xxxv, 399.
20. Deaver: The Significance of Upper Abdominal Symptoms, *Charlotte, N. C., Med. Jour.*, 1915, lxxii, 169-179.

THE OPAQUE MEAL VERSUS THE STOMACH TUBE IN THE DIAGNOSIS OF GASTRIC HYPOMOTILITY.¹

BY I. H. LEVY, M.D.,

PROFESSOR OF MEDICINE, SYRACUSE UNIVERSITY, SYRACUSE, N. Y.

It is generally conceded that the motor function of the stomach is of greater importance than either its digestive or absorptive. Anything interfering with its normal emptying interferes with the general process of digestion. Hypomotility, as I use the term, does

¹ Read by title at the annual meeting of the American Gastro-enterological Society at Atlantic City, May 6, 1918.

not refer to a lowered muscle tone, but a failure of the stomach, whatever the cause may be, to get a meal into the intestine within a definite time, known as normal. It is well known that stomachs differ in size and rapidity of digestion, and that a number of factors, like kind of food, size of meal, position, mental state, etc., modify the evacuation time. However, delay beyond a certain period becomes pathological. There is, as yet, no uniformly accepted procedure for determining the gastric emptying time. It is, however, common practice to consider food found in the stomach in the morning after a hearty evening meal as indicative of a severe grade of motor insufficiency. Food found in the stomach seven hours after an ordinary meal is diagnostic of the milder grades.

The roentgen-ray diagnosis is based on a residue six hours after the ingestion of an opaque meal. Unfortunately, however, no standard technic has been followed by roentgenologists. The kind and quantity of the opaque salt used differs. Some use a liquid vehicle like buttermilk or cocoa, others a more solid one like bread and milk or cereal. The amount of opaque salt varies from two to six ounces; the total amount of the meal from six to twenty. There is even no uniformity of practice in regard to eating between the first and six-hour observation, nor is the stomach always emptied previous to beginning the examination. Conclusions drawn from such diverse procedures should not be contrasted. The technic of the opaque meal should be standardized, like the Boas test breakfast.

Two years ago I reported, with Dr. Kantor,² 185 cases of delayed gastric emptying occurring in an unselected series of 1600 patients with digestive symptoms. I am now able to report 1000 additional cases studied both with the tube and the roentgen rays.

TECHNIC. After a complete history and physical examination the patient presents himself in the morning fasting. The tube is introduced and the contents aspirated. The Ewald test breakfast is then administered and extracted one hour later. Occasionally the Rehfuß fractional method is employed. The roentgen-ray examination follows. The meal consists of 100 gm. of barium sulphate in 500 c.c. of buttermilk. The usual fluoroscopic and radiographic examination is made and the patient instructed to return in six hours and warned not to eat or drink in the interval. On the following day he is requested to eat a regular meal consisting of meat, potato, bread and some light dessert, the quantity to correspond with what he usually consumes at dinner and to present himself seven hours later, not eating or drinking in the interval. The object of the visit is not disclosed so as to eliminate the psychic factor. The tube is then introduced, the contents aspirated and the stomach washed out. As the stomach should be empty at this time the amount of residue determines the degree of motor disturbance.

² A Clinical Study of Delayed Gastric Emptying, *Arch. Int. Med.*, 1916, xvii, 476.

Analysis of the 1000 cases showed hypomotility, with the opaque meal, 100 times, with the tube, 141. In no single instance did I fail to find some food in the stomach with the tube when any of the opaque meal was visible six hours after. Occasionally the tube rest was less than the opaque meal rest indicated. On the other hand in 41 cases the tube gave evidence of delayed emptying when the roentgen-ray method failed to discover any residue. As a rule these cases are of the milder forms of motor disturbance. However, there were 9 cases in this group with a typical duodenal ulcer history. Two of these were verified at operation. There was 1 case of gastric ulcer also proved at operation. There were 8 cases of chronic appendicitis. Four of these were operated and the diagnosis verified. I believe that chronic appendicitis is very frequently associated with a mild form of hypomotility sufficient to give a moderate seven-hour rest with a Riegel meal but none with the six-hour opaque. But besides these 41 cases there were 22 others that gave but a minimum six-hour roentgen-ray rest in which the tube showed a large rest—in one case as much as 800 c.c. and in a number of others over 150 c.c. From the above study I would conclude that the seven-hour tube test is superior to the six-hour opaque meal method as practised by roentgenologists in the diagnosis of gastric hypomotility, for in 28 per cent. of the cases it gave evidence of a rest not discovered by the roentgen-ray method and in 17 per cent. more it showed a marked hypomotility when the roentgen-ray method indicated but a slight disturbance. In both groups there were a number of surgical conditions.

I am aware that these conclusions are not in accord with those of Carman and Miller,³ of the Mayo Clinic. They state that "During the year 1914, 950 patients who had been examined both by the roentgen ray and the test meal went to operation; 220 of these, or 23.1 per cent., showed a gastric residue at the roentgen-ray examination from the six-hour meal; 131, or 13.7 per cent., had food remnants. In other words the roentgen ray showed approximately 70 per cent. more retentions than did the clinical test meal." In attempting to explain the discrepancy between the tube and roentgen-ray findings, Carman and Miller say: "It would seem probable the time elapsing between the ingestion of the gastro-enterologist's meal and that its withdrawal is too liberal and pathological hypomotility excited." I believe this explanation hits the nail on the head. It is hardly just to compare a six-hour opaque meal residue with a fourteen- to sixteen-hour tube one. A stomach may suffer from a decided degree of hypomotility and yet manage to empty itself during the night. The six-hour opaque meal and the "fasting contents" rest may be sufficient to detect gross surgical lesions, but they are not delicate enough for all clinical purposes.

³ The Roentgenological Determination of Gastric Motility, *Arch. Int. Med.*, 1915, xvi, 406. The Roentgen Diagnosis of Diseases of the Alimentary Tract, Philadelphia.

For the clinician, even in the non-surgical conditions, it is important to recognize these cases of hypomotility, as they give rise to definite symptoms. The stomach should be empty of one meal before the next is introduced. The healthy stomach is capable of a great deal of abuse. It can tolerate a second meal on top of the previous one. However, the digestive juices at the end of a meal are not quite the same as at the beginning. In a stagnating stomach six or seven hours after a meal the contents are decidedly abnormal. There may be fermentation, the odor is frequently foul and rancid and abnormal products of digestion formed. Pouring fresh food into such a stomach at once leads to the souring of the fresh meal. These patients suffer from fulness, belching and a variety of toxic symptoms. They believe the food eaten at the last meal responsible for their distress. It is not the last meal but the remains of the previous one that produce the symptoms.

Harmer and Dodd⁴ call attention to the difficulty of always emptying the stomach with the ordinary tube, but, despite their contention, it is my opinion that with a properly constructed tube, a proper technic and a bulb extractor the stomach can, with very rare exceptions, be emptied of its contents.

It might be suggested that the roentgen-ray method could be made more delicate by shortening the emptying time from six to four hours or even less. Or the roentgen-ray method might be combined with the Riegel method as suggested by Cole.⁵ He says: "In a previous communication⁶ I have already shown the fallacy of testing the gastric motor efficiency by administering bismuth suspended in fluid or mixed with cereal, and the same is true for intestinal motor efficiency. If the test is to be of value the stomach and intestines must be called upon to evacuate such a meal as is normally imposed upon them. Therefore the true test of gastro-intestinal motor efficiency is made by administering bismuth or bariun, suspended in fluid, but preferably buttermilk, in conjunction with a Riegel meal of meat, potatoes and bread."

To shorten the roentgen-ray method, I believe, would be unwise, as roentgenologists, as a rule, are rather more particularly interested in the discovery of actual lesions than functional disturbances. Too much surgery is now being done on misinterpreted roentgen-ray evidence, and to shorten the time would increase the evil. I am in accord with Bassler,⁷ who states: "It is apparent, whatever has been advanced to the contrary, that the method of examination by food

⁴ Sources of Error in the Use of the Stomach Tube for Diagnosis: Preliminary Report, *Arch. Int. Med.*, 1913, xii, 488.

⁵ Relation of Lesions of the Small Intestine to Disorders of the Stomach and Cap as Observed Roentgenologically, *AM. JOUR. MED. SC.*, 1914, cxlviii, 92.

⁶ Die Diagnose der Boesartigen und Gutartigen Magen- und Duodenal-Laesionen und ihre Unterscheidung durch Serien-Roentgen-Aufnahmen, *Ztschr. f. klin. Med.*, Berlin, 1914, B. lxxix, H. 5 u. 6.

⁷ Some Recent Conclusions on Abdominal Roentgen-ray Work, *Jour. Am. Med. Assn.*, 1913, p. 213.

extraction is decidedly more to be depended on in gaining an idea of exit from the stomach than is the bismuth roentgen-ray method." But the most serious objection to the opaque meal as a test for hypomotility is that these salts do not enter into the human dietary. For practical purposes it matters very little how long these substances remain in the stomach. It would seem more rational to test its motor function by giving the patient a meal he is in the habit of eating. If the roentgen-ray method simply determined the length of time that an opaque meal remained in the stomach its use could entirely be dispensed with. This could be determined just as well with the tube and the patient spared the expense and the physician the danger of roentgen-ray exposures. To accomplish this it would only be necessary to substitute the Rieder meal for the Riegel. The opaque meal could be administered as for roentgen-ray work. The tube could be introduced six hours later and the amount of opaque salts remaining could actually be measured and weighed; or, better yet, the fractional extraction method of Rehfuß could be used and the exact time the bismuth remained in the stomach determined.⁸

But the tube tells us more than that a rest is present. From the character of the residue we learn whether the patient masticates his food thoroughly; just what food is difficult for him to expel; whether abnormal products of digestion are present; whether fermentation is taking place and whether there is hemorrhage—all this information is easily obtained and is valuable in diagnosis and treatment.

It is not my intention to belittle in any way the importance of the roentgen-ray diagnosis of gastro-intestinal conditions, nor do I advocate disregarding the roentgen-ray evidence in hypomotility. It is simply my purpose to emphasize that a rational test for gastric emptying should be based on a meal of ordinary bulk and complexity which the patient should dispose of in seven hours, and that the roentgen-ray test as commonly practised is not sufficiently delicate for many clinical purposes.

APLASTIC ANEMIA.¹

BY J. P. SCHNEIDER, M.D.,

ASSISTANT PROFESSOR OF MEDICINE, UNIVERSITY OF MINNESOTA MEDICAL SCHOOL.

APLASTIC anemia, so named by Ehrlich in 1888, is classified by Türk among the hemolytic anemias, largely on the grounds of resemblance of one case to his Typus S and by Morawitz as an

⁸ Robin uses such a meal. He administers 1 gm. of bismuth subnitrate with a simple meal in the evening and aspirates in the morning. He says: "In the normal we either find none or at most an occasional crystal of bismuth subnitrate. In cases of motor insufficiency we find in the fasting stomach many dark brown crystals of bismuth sulphate," *Arch. f. Verdauungskrankheiten*, 1907, 438.

¹ Read before the University Medical Society, February, 1918.

"anemia dependent upon decreased blood formation." Barker adapts the latter's classification and refers to it as an "aregeneratory or aplastic anemia of unknown origin." While in many cases this is as yet unfortunately true, there have been reported in the literature true-to-type cases in which a definite etiological factor appeared to be present. Dalton reports the type blood and clinical picture, with suppuration about the jaws, Schilling, working in the tropics, as accompanying black-water fever and sprue, while in benzol poisoning, studied clinically by Selling and imitated in animal experimentation, the brunt of the toxic effect fell without doubt upon the marrow, both leukopoietic and erythropoietic tissue undergoing destruction. In Parkes Weber's case, reported in 1914, there was at the onset gingival stomatitis, rapidly spreading on to the right cheek and there forming a definite phlegmonous induration, pyrexia and an aplastic type of anemia progressing to a rapid end in ten weeks. We cannot here, as in the acute leukemias, explain away the phlegmon by a supposed local leukemic infiltration. The postmortem examination in Weber's case showed no hyperplastic red marrow, as it should in a hemolytic infection.

During the past three decades some 60 cases of aplastic anemia have been reported. Among these are 12, with considerable evidence for the establishment of certain gross lesions as probably etiological. Sufficient evidence, Musser thinks, to warrant our definition being henceforth: an anemia secondary to marrow changes dependent upon some known or unknown cause.

In the older literature there appears frequently the conception that a fulmination hemorrhage is etiological, in that it leads to an exhaustion of the marrow. Today we are convinced that such hemorrhages are purely symptomatic. To explain away the fact that a severe hemorrhage did not lead to aplastic anemia in all instances, it was cited that the constitution of the individual determined the issue—namely, the hypoplastic individual would fail to deliver new blood in adequate measure. There are quite as many cases reported as occurring in normal-type individuals as in such as at the post-mortem table give evidence of mesoblastic hypoplasia.

While etiologically we are still in the dark, there is no question of the propriety of giving aplastic anemia a separate and distinct pigeon-hole among the anemias due to decreased blood formation—clinically, hematologically, anatomically, as well as from the derived pigment studies it stands quite on its own legs. I, for one, object to referring to aplastic anemia as idiopathic pernicious anemia, aplastic variety. Pernicious anemia stands at one pole, aplastic at the other; to make of one a variety of the other is simply to introduce confusion. As an entity, aplastic anemia presents the following aspects:

1. May occur at any age, extremes reported 5.7 to 68 years. Most frequent in early adult life.

2. Sex incidence in proportion of 20 males to 15 females.
3. Rapid, non-remittent course 2 weeks to 1½ years, average 6 months.
4. Skin pale gray, not straw yellow or waxy, as in pernicious.
5. Sclera never icteric nor urine highly pigmented.
6. Strikingly leukopenia as low as 140, average below 2000, a relative increase of lymphocytes only.
7. Extraordinary reduction in blood-platelet count, often to 20 to 25 per cent. of normal.
8. The consequent presence early of a marked hemorrhagic tendency.
9. Presence of fever frequently reaching a high point.
10. No enlargement of liver or spleen.
11. No painful bone-pressure phenomenon.
12. No megalocytosis, marked poikilocytosis, polychromasia or basophilic granulation.
13. Practical absence at any stage of erythroblasts.
14. At the postmortem examination characteristic punctate hemorrhages in practically all subserous and subperitoneal surfaces and the absence of hyperplastic marrow changes.
15. Duodenal pigment values are subnormal, urobilinogen absent, urobilin less than normal and bilirubin reduced in proportion to the degree of anemia.

I wish to report 3 cases of aplastic anemia coming under my observation during the past four years:

CASE I.—Female, Jewish nationality, aged twenty-six years, married. Family history negative. No severe illness in the past except measles while a child. Felt well and looked well until August or September, when the patient was observed by her friends to be pale. On November 15 she married. On December 24, at her normal menstrual period, she menstruated profusely until December 30. She became very pale. However, on December 15, the presence of bleeding gums was noted. On January 4 a severe epistaxis supervened; a tampon did not succeed in controlling the bleeding, hence the patient was sent to the hospital, and from the nose and throat clinic was referred to the medical clinic. On January 12 the bleeding was less but persistent. The intravenous introduction of gelatin apparently was followed by fever. On January 16 the patient was semicomatose, very pale—not lemon color—a peculiar dirty gray skin, especially at such places as the skin had been subjected to pressure. The gums, nasal surfaces, soft palate and skin, especially of prominent parts of the legs and arms, showed submucous and subcutaneous varicolored hemorrhagic areas. No icterus was present in the sclera. Temperature, 103°. Pulse, 120. Patient vomited; no blood, fresh or altered. Over the precordium a soft systolic murmur was noted. Both lower

lung borders were atelectatic. Spleen and liver were not enlarged. Systolic blood-pressure, 100.

Blood Examination. Blood hydremic, $\frac{1}{8}$ solid, $\frac{7}{8}$ fluid. No nucleated red cells. Platelets not counted. Red blood cells, 1,240,000; coagulation time normal. White blood cells, 1600; bleeding time prolonged. Hemoglobin, 18 per cent. Index, 0.7.

Urine. Light color; trace of albumin; no urobilinogen or urobilin.

Duodenal Contents. Duodenal siphonage revealed light yellow contents, giving no qualitative test for urobilinogen.

Stool. Guaiac, negative.

Horse serum was administered for three days, with no effect, and the patient died on January 20, less than one month after the immediate onset, with bleeding gums; however, probably five or six months after the actual insidious remote onset.

Postmortem Findings on January 20 (day of death). 1. The usual punctuate hemorrhages.

2. Persistent thymus—weight, 30 grams—apparently a status thymicolymphaticus.

3. Femur and humerus alone examined. In only the proximal one-third occasional small pink areas in an otherwise pale yellow marrow. Microscopically myeloblastic tissue, occasional normoblasts, with many of the progenitors of both the above in a state of almost unrecognizable degeneration.

4. Uterus, no lesion; small; hypoplastic. (No note was made relative to the absence or presence of hemosiderosis in the liver or the spleen.)

CASE II.—This patient, an unmarried female blonde, aged seventeen years, had an uneventful family and past history, except that she menstruated scantily since the onset of this function at fifteen. Six days before entrance she began to menstruate at the proper time, but profusely; seventy-two hours later epistaxis began and the next day the gums began to ooze. Tamponage did not succeed in controlling the nasal bleeding, and the nasal seepage was rather foul.

Physical examination revealed a light-complexioned female of asthenic habitus, fairly well nourished. The sclerae were pale blue and not icteric. In all of the mucous membranes of the mouth and throat, so far as visible, there were bleeding areas. On the legs arms under the skin there were numerous varicolored hemorrhagic areas, and from the presence of deep-lying hard areas we gather there were hemorrhages in the areolar tissues between the muscles.

Three days later this patient died in spite of many attempts to control the bleeding. No blood examination other than a rough bedside one was made. This gave a red blood count of 1,200,000; hemoglobin, 15; white blood count, 900. No postmortem was obtained.

CASE III.—This patient was seen during the past year and presented a very interesting but sad spectacle. Mrs. H., a grass widow, aged forty-seven years, American nationality, was referred to me by Dr. H. Z. Giffin, of the Rochester Clinic, on July 10, 1917. Her complaint was of weakness, palpitation and dyspnea.

Family History. Her father died at forty-nine years of dropsy; her mother at fifty-nine years of a chronic lung complaint; two brothers, one at twenty-two and the other at twenty-three years, died of phthisis; one sister, older, died of a probable phthisis. Her husband was of loose habits and had not lived with the patient for eleven years.

Past History. At ten years she had measles and pertussis. At twenty-three years she was in bed one week with what was considered a pleurisy. During the winter of 1902 she had probable epidemic influenza. During her brief married life she had no living or term child, but had one miscarriage at two and a half months. Her menstrual cycle has always been of the twenty-one day type, and that has not altered until the past two periods, when the amount has been decidedly greater. In July, 1913, a tumor was removed from her right breast. On September 29, 1913, the left breast and axillary glands were excised at Rochester. The pathological examination showed a chronic cystic mastitis. She gave no evidence of anemia at this time.

Present Illness. On April 19, 1917, she was again examined at Rochester for a sore mouth, which was stated to have begun three weeks before, following a severe "cold in the head." A Wassermann test was negative and a smear from the roof of the mouth showed the organisms of Vincent's angina. While under treatment she became pale and on May 2 her blood count was as follows: Hemoglobin, 48 per cent.; red blood cells, 3,060,000; white blood cells, 2200; color index, 0.7. Differential count: Polymorphonuclears, 4.3 per cent.; small lymphocytes, 92.3 per cent.; large lymphocytes, 3.3 per cent. Anisocytosis and poikilocytosis of slight degree.

On May 7 the hemoglobin stood at 45; red blood cells, 2,830,000; white blood cells, 1600. Differential count as above.

On June 26 the hemoglobin had fallen to 40 per cent.; red blood cells, 2,500,000; white blood cells, 1800. Differential count: Polymorphonuclears, 7.5 per cent.; small lymphocytes, 74.5 per cent.; large lymphocytes, 18 per cent. Six normoblasts were seen; also moderate poikilocytosis and anisocytosis.

Glands and spleen were not palpable and the general physical examination was negative. On May 8 a detailed neurological examination was negative.

At my first examination of the patient, on July 10, she gave the appearance of decided pallor, withal well nourished. There was no icterus of the sclera. The routine physical examination revealed

no organic findings. The spleen and liver were not palpable nor the glands enlarged. There were no petechiæ visible on the exposed mucous or skin surfaces. The blood findings of this date gave: Hemoglobin, 40 per cent.; red blood cells, 2,000,000; white blood cells, 2600; polymorphonuclears, 15 per cent.; large lymphocytes, 15 per cent.; small lymphocytes, 55 per cent. There were no normoblasts or polychromatophilia. The gastric secretory and motor function was normal.

On July 11 a duodenal contents was secured. It was at the conclusion of this procedure, after lying on her right side for an hour and a half, that the first striking clue to the type of her anemia was revealed in the nature of myriads of subcutaneous hemorrhages on all the skin surfaces exposed to the pressure of the table. These were particularly abundant in the face.

Acting on this clue a blood platelet count was immediately made revealing a count of 90,000.

The duodenal contents were secured in the amount of 40 c.c. It was dark yellow, of alkaline reaction (the acid spurts having been carefully segregated), containing no macroscopic sediment. Urobilinogen, none; urobilin, 800 units;² bilirubin, 2+. This, I believe, is the first quantitative duodenal pigment study done in an aplastic anemia.

Our patient was immediately sent home and put in bed and application was made for admission to the University Hospital. Two days later a profuse menorrhagia began, the control of which proved futile.

Admission to the hospital dated from July 23, 1917.

Hospital Record (Mrs. N. H.). Complaints: Anemia, weakness, loss of weight, menorrhagia, nicturia, stomatitis.

Physical Examination. Paleness of the skin and the mucous membranes; lemon-yellow color to the skin over the exposed parts. Numerous ecchymoses over the trunk and especially over the extremities. Surgical scars on the chest from the breast removal. Gingivitis; tonsils submerged, not seemingly pathological. Blowing systolic murmur heard only over the precordium and pulmonic area (hemic). Increased knee-jerks and a double short ankle-clonus. Eye-grounds: disks pale; numerous large and small hemorrhages along the course of the vessels, both inside and outside of the disks. Bleeding profuse from the uterus; uterus retroverted. Blood-pressure, 128.58. Pulse, 90 to 120. Temperature normal to 102°.

Laboratory Data. Urine entirely negative. Blood Wassermann negative. Capillary resistance low. Petechiæ after two minutes. Blood platelet count, 72,000 (August 1, 1917). No reticulated reds ever found. Blood examinations.

² Schneider, J. P.: The Splenic Pathology of Pernicious Anemia and Allied Conditions, Arch. Int. Med., 1916, xvii, 32.

July 27: Hemoglobin, 25 per cent.; white blood cells, 3100; red blood cells, 1,821,000.

July 31: Hemoglobin, 17 per cent.; white blood cells, 2800; red blood cells, 948,000; polymorphonuclears, 10 per cent.; lymphocytes, 44 per cent.; large mononuclears, 30 per cent.; transitionals, 6 per cent.; degenerated reds, 10 per cent.; size of reds, 7 mikra; stain of reds, pale; anisco, very slight; poikilocytosis, slight; polychromatophilia, slight; nuclear reds, none.

August 2: Hemoglobin, 24 per cent.; polymorphonuclears, 4 per cent.; lymphocytes, 6 per cent.; large mononuclears, 68 per cent.; transitionals, 10 per cent.; degenerated reds, 12 per cent.; size of reds, 7 mikra; stain of reds, pale; anisco, very slight; poikilocytosis, slight; polychromatophilia, slight; nuclear reds, none.

August 3: Hemoglobin, 12 per cent. (after transfusion, 24 per cent.).

August 6: Hemoglobin, 20 per cent.; white blood cells, 1600; red blood cells, 968,000; polymorphonuclears, 23 per cent.; lymphocytes, 26 per cent.; large mononuclears, 38 per cent.; transitionals, 8 per cent.; degenerated reds, 5 per cent.; size of reds, variable; stain of reds, pale; anisco, none; poikilocytosis, slight; polychromatophilia, none; nuclear reds, none.

August 7: Hemoglobin, 15 per cent.; red blood cells, 850,000.

August 9: Hemoglobin, 12 per cent.; white blood cells, 1400; red blood cells, 768,000; polymorphonuclears, 8 per cent.; lymphocytes, 42 per cent.; large mononuclears, 47 per cent.; transitionals, 3 per cent.; size of reds, normal; stain of reds, pale; anisco, none; poikilocytosis, slight; polychromatophilia, none; nuclear reds, none.

Important Therapeutic Data. Ergot, calcium, blood serum and whole serum given on several occasions. Blood transfusion, 300 c.c. (citrate method) on August 3, and again 400 c.c. on August 6, with reaction. (Temperature, 103°; pulse, 140.)

Patient died August 10, 1917, four months and ten days after the abrupt onset of what appeared to be a trivial unknown infection of the upper air passages.

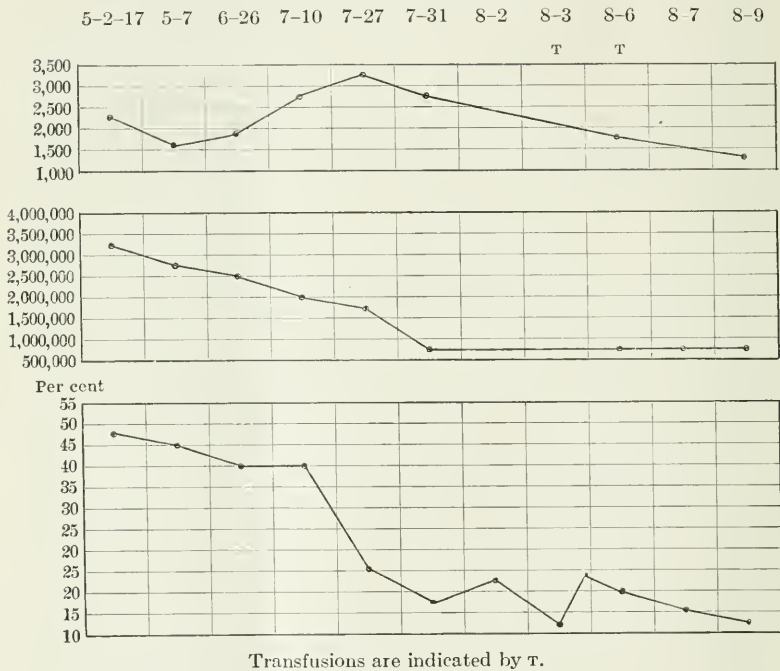
The postmortem data were as follows:

Body well nourished, weighs about 150 pounds. No edema. Skin very pale, with faint yellowish tinge. Small subcutaneous hemorrhages over left arm and both thighs. Subperitoneal hemorrhages on the anterior parietal peritoneum and on the diaphragmatic peritoneum. Old pleuritic adhesions on the left side; 200 c.c. of thin straw-colored fluid in the left pleural cavity; 500 c.c. of similar fluid in the right cavity. The pericardial cavity contained about 75 c.c. of straw-colored fluid. There were a few subpericardial hemorrhages on the right auricle. The heart weighed 300 grams. Musculature was light yellowish brown and rather soft. Areas of fatty degeneration of the muscle under the endocardium, giving a "tabby-cat" appearance. Normal valve leaflets. Lungs, small

amount of bronchopneumonia. Spleen weighed 160 grams. Smooth capsule. Rather firm reddish-brown pulp. Liver weighed 1400 grams. Cut surface light yellowish brown in color. In the kidneys there were no gross changes except some submucous hemorrhages in the pelves. There were several cysts in the ovaries. No examination of the head or the long bones.

Microscopic examination of the spleen showed in nearly all the follicles some areas of hyaline degeneration of the stroma. The arteries are apparently not involved.

CHART SHOWING VARIATIONS OF WHITE BLOOD CELLS, RED BLOOD CELLS AND HEMOGLOBIN IN CASE III.



SUMMARY. 1. All three of these cases of aplastic anemia occurred in females.

2. Two were definite asthenics, with a 30-gram thymus at the age of twenty-six years in one. One was of normal habitus.

3. A definite history of a remote stomatitis or "cold in the head" is absent in 1 and 2 but present in 3. Between this and the fulminating onset with hemorrhagic symptoms there was a period of three and a half months of progressive anemia in 3, and this period of insidiously but rapidly developing anemia was also present in 1 and 2.

4. In Case III, in the Rochester reports of the May 7 blood examination, a half-dozen normoblasts were seen. This is exceptional, but occurs in one other reported case of Türk's series.

5. All three had a marked leukopenia, increasing in degree toward the end.

6. The platelet count was low but no definite figures were preserved in Case I. In Case II no blood examination was made. In Case III, 90,000 and later 72,000.

7. All three were free of clinical evidence of excessive blood destruction: pale sclera, pale urine and small liver and spleen.

8. At the postmortem examination of Case I the marrow of the long bones presented no hyperplastic attempts. No note is made of the spleen and liver. In Case III, while the long bones were unfortunately not examined, the spleen and liver were less than normal in size in an otherwise well-nourished individual.

9. The duodenal contents were qualitatively studied in Case I, urobilinogen being absent and the gross color excluding an abnormal amount of urobilin. In Case III the values obtained in the duodenal contents were precisely those found in a non-hemolytic anemia, an oligochromia. In a pernicious type, with a count of 2,000,000, the duodenal values of urobilin and urobilinogen would have been several thousands units. The H-H index³ of 0.46 speaks for a total absence of marrow delivery. That the hemosiderosis occasionally reported present in the liver in aplastic anemia is not due to hypersplenism is probable from these values. That it is due to absorption of extravasated blood from the various hemorrhagic areas is probable, but remains to be proved. A duodenal pigment study is advisable in the differential diagnosis of aplastic as against the hemolytic anemias.

10. Table I represents graphically the progressive downward course of the disease uninfluenced by transfusion.

11. The hemorrhagic feature, distinctly purpuric in character, is linked up with the reduced platelet supply, Hurwitz's studies having shown the parallelism existing between the platelet count and bleeding time. The fragility of the vessels themselves is less easy of comprehension.

12. Viewed in the light of the above findings and influenced by the postmortem observations of Engel and Hirschfeld, I feel that proper emphasis should be placed upon the fact of toxic marrow destruction, in a reconsideration of the terms by which this disease is known. Aplastic anemia implies congenital defect. Hypoplastic and aregeneratory imply poorly developed marrow readily failing on demand. A better term would be toxic paralytic anemia or toxic anhemopoietic anemia.

³ Schneider, J. P.: Further Quantitative Study of the Duodenal Blood-derived Pigments, *Arch. Int. Med.*, 1917, xix, 1.

* Ueber aplastische Anämie, *folio Hematol.*, Leipzig, 1911, xii, 347-362.

THE DIAGNOSIS AND TREATMENT OF DIAPHRAGMATIC PLEURISY: WITH REPORT OF CASES.

By T. H. KELLY, B.S., M.D.,

INSTRUCTOR IN MEDICINE, UNIVERSITY OF CINCINNATI; ASSISTANT ATTENDING PHYSICIAN, CINCINNATI GENERAL HOSPITAL,

AND

H. B. WEISS, A.B., M.D.,

INSTRUCTOR IN MEDICINE, UNIVERSITY OF CINCINNATI; ASSISTANT ATTENDING PHYSICIAN, CINCINNATI GENERAL HOSPITAL; PHYSICIAN IN CHARGE, WILHELM AND GETTE BECKMAN DISPENSARY, CINCINNATI, OHIO.

(From the Department of Internal Medicine, University of Cincinnati, the Medical Clinic of the Cincinnati General Hospital and the Wilhelm and Gette Beckman Dispensary.)

For many years it has been noted that not infrequently a pneumonia begins with symptoms resembling acute abdominal disease, particularly in children. J. P. Crozer Griffith¹ reported several cases, as did also Herrick² and others. Needless to say, many clinicians have suffered the experience of advising operation for some acute intra-abdominal condition, only to find the abdominal contents normal and a pneumonia in one of the patient's lower lobes the day following the operation.

To Capps³ we owe the well-defined picture of involvement of the diaphragm by inflammatory processes. He published in 1911 the results of experimental irritation of the diaphragmatic pleura in a series of human beings, the work being done upon patients with pleural effusions. Irritation of the diaphragm was accomplished by means of a wire introduced through a trocar inserted into the pleural cavity preparatory to the withdrawal of the pleural effusion. His observations covered experiments upon 75 patients, only 35 of whom presented favorable conditions for free exploration of the diaphragm. He also presented in the paper a very complete discussion of the previous work, which has been published upon the innervation of the visceral and parietal pleura.

He concluded from his experiments that:

1. The visceral pleura is not endowed with pain sense.
2. The parietal pleura is richly supplied with sensory fibers from the intercostal nerves and irritation of it produces pain that is accurately localized by the individual over the spot that is touched. Such irritation never gives rise to "referred" pain in the neck or elsewhere.
3. The diaphragmatic pleura receives its nerve supply from the last six intercostal nerves, which supply a peripheral rim of the diaphragm two or three inches wide anteriorly and laterally and a segment corresponding to the posterior third, and from the phrenic nerve which supplies the central portion of the diaphragmatic pleura.

The pain produced by irritation of the central part of the diaphragmatic pleura is a true referred pain, and is distributed over the skin and tissues supplied by the third and fourth cervical segments, with a predilection for the trapezius ridge.

The pain elicited by irritation of the peripheral or posterior portion of the diaphragmatic pleura is also a true "referred" pain. The pain is usually distributed in segmental areas over the lower thorax and epigastrium, sometimes extending downward over the whole abdomen on the same side (seventh to twelfth dorsal segments).

Both pains are spontaneous and are associated with hyperesthesia and hyperalgesia of the skin and superficial tissues on pressure.

4. The pericardial pleura receives its innervation chiefly, if not exclusively, from the phrenic nerve. Irritation of this part of the pleura results in "referred" pain in the neck of the same character as that following irritation of the central portion of the diaphragmatic pleura.

This work offered a definite starting-point from which to work in the diagnosis of involvements of the diaphragmatic pleuræ, and in 1916 Capps⁴ published a series of 61 cases of diaphragmatic pleurisy, in all of which the diagnosis was confirmed either by autopsy or the subsequent history of the cases. In this article he called attention to the various distributions of the referred abdominal pain, and emphasized the points of difference between it and the pain of true abdominal disease.

The skin and muscles of the abdomen are more sensitive in referred pain from the diaphragmatic pleura than in abdominal visceral disease, and the cutaneous reflexes are more lively in referred pain. Deep pressure with the flat hand is better born in referred diaphragmatic pain, while it produces deep pain over an inflamed organ within the abdomen.

The presence of sharp localized pain in the neck, occurring spontaneously or only on pressure, on the same side as the abdominal pain often suggests the true state of affairs, as it indicates irritation of the phrenic nerve. The referred pains in the neck and abdomen are often aggravated by cough or deep breathing.

Also, in acute diaphragmatic disease there are usually present evidences of respiratory infection, such as cough, expectoration, herpes labialis, rapid respiration, high leukocytosis, etc. According to Capps, hiccough is not common in diaphragmatic disease, as was formerly supposed, having occurred only five times in his 61 cases.

The differential diagnosis of involvement of the diaphragmatic pleura and abdominal disease is very important, and at times the clinician is in a veritable whirlpool of indecision concerning the correct diagnosis. We have had the opportunity in the past two years of observing in the Cincinnati General Hospital and the Wilhelm and Gette Beckman Dispensary a number of patients

exhibiting some or all of the features mentioned by Capps in his description of diaphragmatic pleurisy. In certain of these cases the question of surgical intervention was quite acute and the importance of correct diagnosis therefore correspondingly great.

From these cases we have selected 22 in which the diagnosis was confirmed either by their future course or at the autopsy table, and are presenting them, hoping to show the variations in the manifestations of diaphragmatic pleural disease and the different paths by which we arrived at a diagnosis in the different instances. The accompanying table shows the symptoms, both subjective and objective, that were found in our cases. (See Figs. 1, 2, 3.)

Of these 22 cases 10 were acute in character, 3 had acute exacerbation at the time of observation and 9 were subacute or chronic. The following cases in the first group resembled surgical conditions so closely that the question of operative intervention was seriously considered:

No. 1, renal stone; No. 4, acute cholecystitis; No. 6, cholelithiasis with colic; No. 8, generalized acute peritonitis from perforated typhoid ulcer; No. 14, operation was done for an acute appendicitis, much to our chagrin; Nos. 18 and 22 both had operation for gall-bladder disease several years previous to the time of observation. In both cases neither stones nor any other pathological condition were found at operation, and shortly afterward there was a recurrence of the symptoms that had existed before the operation. In the remaining cases of the acute group the symptoms or history immediately gave an inkling as to where the seat of the trouble lay.

In the group of chronic types the question of surgical treatment arose in No. 7, which is interesting because it combined definite symptoms of diaphragmatic pleurisy and a chronic appendicitis, which were both proved by the further history of the case. In the acute cases the symptoms arose suddenly, as with the onset of pneumonia, and after several weeks practically all the symptoms had left. On the other hand, in the chronic cases, the onset was acute and the symptoms subsided, but at irregular intervals there was a recurrence of the symptoms, in whole or in part, usually without an increase in temperature and not with the original acuteness. At these periods of recurrence exertion and cough intensified the symptoms, and frequently exertion was the cause of the recurring attack. The chronic sufferers complained just as bitterly of the pain and, occasionally, of the hyperesthesia as those who suffered from an acute attack.

Hyperalgesia and hyperesthesia were not always marked, being present in 7 cases. The hyperesthesia, when present, was most acute, and one of the patients cried out when the tips of the fingers were passed over the skin. In one patient clothing was almost unbearable. The involvement in hyperesthesia was usually over a large area. (See charts.) Hyperesthesia and hyperalgesia were

Number.	Sex.	Age.	Referred pain.				Acute.	Chronic.	Nausea.	Vomiting.	Friction sounds.	Pneumonia.	Temperature.	White blood cells.	Polynuclears, per cent.	Roentgen rays.
			Hypersaesthesia and hyperaesthesia.	Abdominal.	Neck.	Beneath twelfth rib.										
1	M.	48	..	X	X	X	X	X	X	100.4	22,000	Increased	Definite.	
2	F.	15	..	X	X	X	100.4	20,000	93.0	Definite.	
3	M.	28	..	X	X	X	X	X	101.6	20,000	88.0	Definite.	
4	F.	55	X	X	X	..	103.6	11,800	68.0	Not definite.	
5	M.	52	..	X	X	X	X	..	98.6	5,500	77.5	Definite.	
6	M.	40	..	X	X	X	99.0	4,100	79.0	Definite.	
7	F.	31	..	X	X	X	X	99.0	8,000	80.0	Not definite.	
8	M.	19	..	X	X	105.0	12,800	79.0	Not definite.	
9	M.	36	..	X	X	X	X	X	X	99.6	Definite.	
10	F.	36	..	X	X	X	Definite.	
11	M.	45	..	X	X	X	X	X	Definite.	
12	M.	40	X	Definite.	
13	F.	23	..	X	X	X	X	X	X	101.2	13,200	54.0	Definite.	
14	M.	36	..	X	100.0	13,500	..	Definite.	
15	M.	38	X	X	X	..	102.6	15,200	..	Not definite.	
16	M.	38	X	X	X	X	X	..	102.6	15,200	Increased	Not definite.	
17	M.	32	X	X	X	X	100.2	Not definite.	
18	F.	35	X	X	X	X	99.0	8,800	Increased	Not definite.	
19	F.	14	..	X	X	X	101.2	12,200	70.0	Definite.	
20	M.	43	..	X	X	X	X	..	101.6	9,600	61.0	Definite.	
21	M.	46	..	X	X	X	X	..	101.0	6,800	..	Definite.	
22	F.	38	..	X	X	X	X	X	99.2	14,200	..	Definite.	
Summary	7	19	19	17	2	9	2	7	5	Fourteen definite.	

* Doubtful.

much more apparent in the acute than in the chronic cases as a rule. In the great majority of cases deep abdominal pressure was borne quite well. Spontaneous pain was not always present in the neck when pain on pressure was marked.

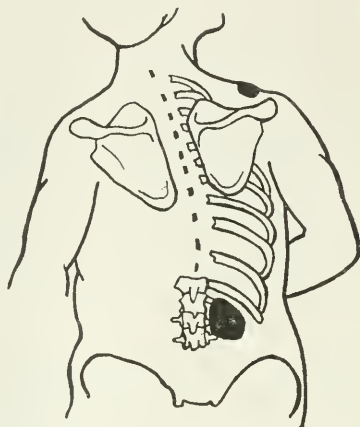


FIG. 1.—Case 1. Showing points of tenderness along the trapezius and beneath the twelfth rib posteriorly.

The two most constant areas of tenderness on pressure were below the twelfth rib posteriorly on the affected side and at the ridge of the trapezius, though the patients did not always complain of

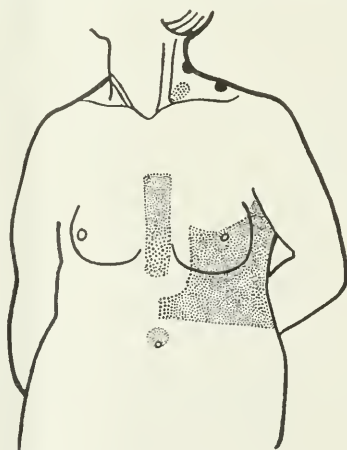


FIG. 2.—Case 2. Showing points of tenderness along the trapezius, in solid marking, and the stippling showing areas of hyperesthesia and hyperalgesia.

spontaneous pain at these points. The upper quadrants of the abdomen were the most frequent sites of the referred abdominal pain. In many of the cases the abdominal pain radiated toward the

flanks, and in two of them there was definite tenderness, involving the entire half of the back from the lower ribs to the ilium. There was usually moderate rigidity and muscle spasm of the abdominal muscles at the areas of referred pain. Abdominal symptoms of

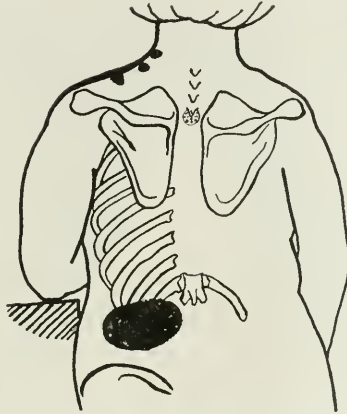


FIG. 3.—Case 3. Showing points of tenderness along the trapezius posteriorly and tenderness beneath the twelfth rib and an area of hyperesthesia over the fourth dorsal spinous process.

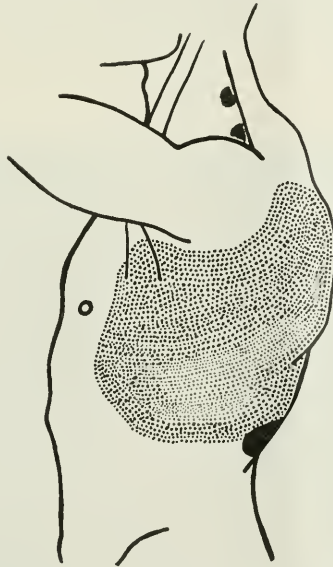


FIG. 4.—Case 12. A lateral view showing areas of hyperesthesia and points of tenderness along the trapezius and beneath the twelfth rib posteriorly.

varying degree were present in 19 of the 22 cases. In 2 cases there was board-like rigidity over the abdomen. One was operated for relief of acute appendicitis and the appendix was found apparently

innocent of any disease. In the other case (No. 8) the rigidity and muscle spasm continued until there appeared definite signs of consolidation in the left base. This is the only patient who died, and at autopsy the pathologist reported: "In the left pleural cavity

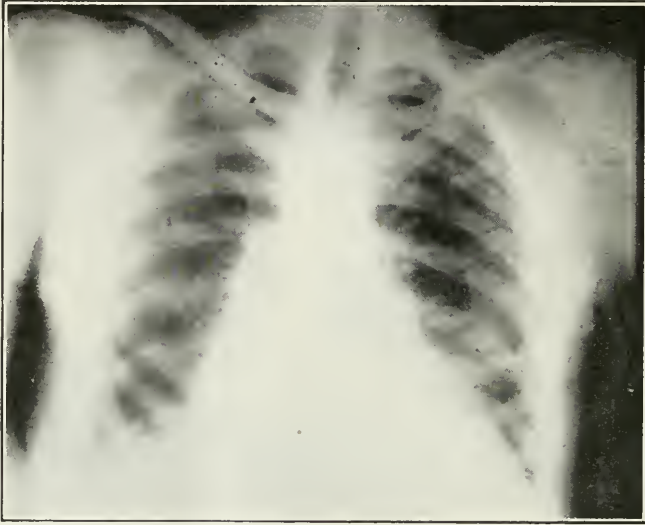


FIG. 5.—Case 1. Roentgen-ray plate showing small area of infiltration over left diaphragm.

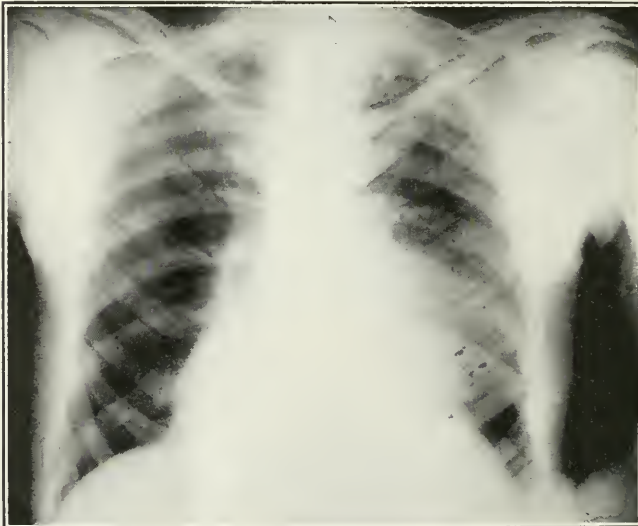


FIG. 6.—Case 1. Showing a definite area of infiltration six days after the first picture was taken.

there were a few acute fibrinous adhesions over the left lower lobe and no fluid. The pleural surface of the left side of the diaphragm

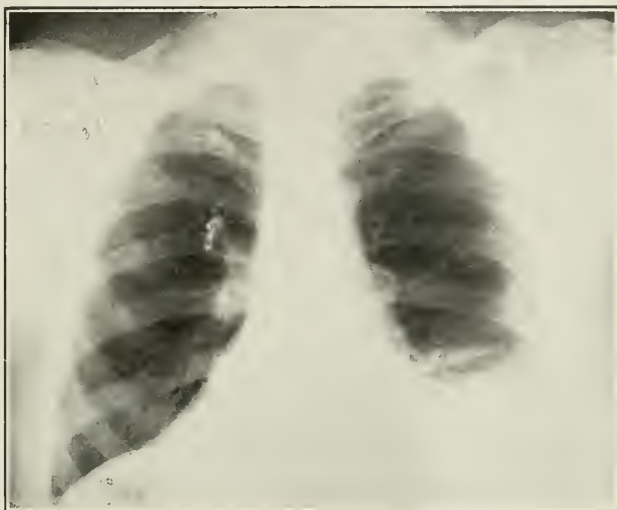


FIG. 7.—Case 6. Showing the position of the diaphragm and markings of the right lower base. One month after this plate was taken another pair of stereoscopic plates "failed to show the shadows at the right base which were seen on the previous plates."

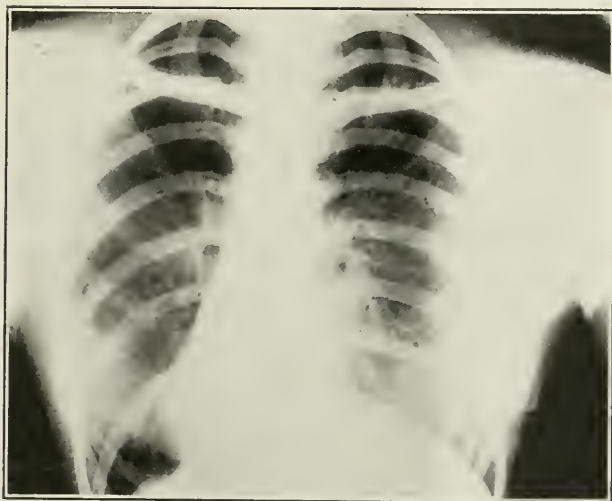


FIG. 8.—Case 13. Showing distortion of the left diaphragm by adhesions.

was congested and had about its middle point and extending posteriorly from this a small amount of fibrin, some of which was under-

going organization. Beneath this and surrounding it there was exceedingly well-marked venous congestion. The peritoneal surface of the diaphragm showed nothing but slight congestion. The lower lobe of the left lung showed a diffuse lobar consolidation, and all of the bronchi of this lobe were filled with pus. There were no abnormal findings in the abdomen."

Capps states that in his series of 65 cases hiccough appeared in only 5 cases, while in our 22 cases this symptom occurred in 2 cases, and in both was quite intractable, all of the usual methods for its relief failing, the hiccoughs apparently ceasing spontaneously.

Fourteen of our cases were males and 8 were females. Gastric symptoms were not frequent. One case showed both nausea and vomiting, while nausea and vomiting were present, each once, in separate cases. In 7 cases friction sounds were heard, practically all in the lower axillary region of the affected side. These friction sounds were probably due to an associated involvement of the costal pleura. Five patients had pneumonia associated with their pleurisy. In the majority of the acute cases there was a rise in temperature, though not very high. The leukocyte count was increased, depending on the acuity of the symptoms as a rule; associated with the increase in leukocytes there was a proportionate rise in the polymorphonuclear neutrophile cell count.

In but 4 of the 19 cases examined by the roentgen rays there were no findings suggestive of pleural or pulmonary involvement. The roentgen-ray findings varied, ranging from definite distortion of the diaphragmatic contours to merely a definite increase of the hilum markings radiating to the border of the diaphragm. In several instances, shadows suggesting calcification were lying close to the diaphragm. In two of the accompanying reproductions of roentgen-ray plates one can see in the early picture a finger-like infiltration above the diaphragm and in the latter picture the shadow of a definite infiltration of the lung in the same region.

The diagnosis of diaphragmatic pleurisy was usually made on the occurrence of pain in the side, associated with pain beneath the twelfth rib on the affected side and along the edge of the trapezius on that side. The pain may be spontaneous in the neck and was so in one-third of our cases. In 19 out of 22 cases there was tenderness along the edge of the trapezius. There is almost a constant finding of tenderness on pressure beneath the twelfth rib posteriorly on the affected side; this symptom was present 19 times in 22 cases. In the vast majority of the cases there is referred pain in the abdomen, with varying degrees of muscle spasm and rigidity. A moderate rise in temperature with an increase in the leukocytes and polymorphonuclear cells is usually present. In some cases there are heart friction sounds in the lower axilla.

The roentgen-ray examination of the chest in over three-fourths of the cases did *show* definite diaphragmatic involvement or pulmonary involvement close to the diaphragm.

In chronic cases there is exacerbation of the characteristic symptoms on exertion, cough and frequently on deep inspiration.

TREATMENT. In the acute cases the treatment is that of any pleuritis. We have found that cold applications, in the form of iced-linen strips, applied (and frequently changed) to the affected side for two hours, is most efficacious. Of course, sedatives are used when necessary. Strapping the lower chest and upper abdomen seems to give the greatest relief, and many of our chronic cases return to us asking that their sides be strapped. They have found that after the side has been strapped their pains will be relieved almost immediately and that they will be free from their annoying symptoms for from several weeks to months.

We are indebted to Mr. R. Isaacs for the accompanying charts.

BIBLIOGRAPHY.

1. Griffith: Jour. Am. Med. Assn., 1903, xi, 531.
2. Herrick: Jour. Am. Med. Assn., 1903, xi, 535.
3. Capps: Arch. Int. Med., 1911, No. 6, viii, 717.
4. Capps: AM. JOUR. MED. SC., 1916, No. 3, cli, 333.

THE FRACTIONAL EXAMINATION OF THE DUODENAL CONTENTS.¹

BY MAX EINHORN, M.D.,

PROFESSOR OF MEDICINE AT THE NEW YORK POSTGRADUATE MEDICAL SCHOOL,
NEW YORK.

THE duodenal contents are of intrinsic value for the welfare of the organism. The main process of digestion is accomplished by the proper working and correlation of the different fluids entering into this comparatively small part of the digestive apparatus (the duodenum). It is quite natural that a study of these secretions from every possible viewpoint will prove useful physiologically as well as pathologically.

In several previous communications I published my results concerning the examination of the duodenal contents. Usually these explorations of the duodenal secretions had been done either in the fasting condition of the patient or some time after the ingestion of either tea and sugar or bouillon. No particular attention had been paid as to the length of time after the meal the examination had been performed.

It appeared to me worth while to undertake a comparative

¹ Read before the Association of American Physicians, at Atlantic City, N. J., May, 1918.

study between the results of the examination in the fasting condition and at different periods after certain test meals. Inasmuch as the duodenal tube must have a comparatively narrow lumen, solid food, even mechanically well comminuted, would be apt to clog up the instrument, and would therefore be inappropriate for these examinations.

For these reasons I had already formerly employed either tea and sugar or bouillon as preparatory meals.

In the present investigation I selected a cup of beef bouillon (one bouillon cube, usually Armour & Co., to one cup of hot water) as the proper test meal. Beef being a strong stimulant for the digestive secretions seemed to answer well our purpose.

Examination of the duodenal contents was first made in the fasting condition, then a cup of beef bouillon was given by mouth and the duodenal contents aspirated every half-hour for a period of two hours (fractional examination).

In order to have a larger collection of cases, we utilized many patients who were on duodenal alimentation or duodenal fluid instillation for this purpose. In these cases the explorations can be carried out with the greatest ease, for they have the tube already in the right place. But we also took patients not accustomed to the tube, principally in conditions in which the bile or pancreatic secretions had to be examined any way. We also had two persons without any subjective symptoms, representing the normal, who were willing to undergo this examination for the benefit of science (George C. and Miss Ruth M., to whom I express my thanks for coöperation).

In all these additional cases the mode of procedure was as follows: The patient was given the duodenal tube in the evening after a light supper. Attention was paid to the length of tube which had entered the buccal cavity before retiring. Mark III of the tube should have reached the mouth; if not, the patient is given milk or water and the tube in this way made to go in beyond the III mark before going to sleep. In patients who sleep restlessly it is advisable to attach the tube, lying outside the mouth, with a piece of adhesive plaster to the cheek, in order to avoid a pulling out of the instrument during the night by any inadvertent motion. In the early morning the capsule end of the tube has usually reached the duodenum and the desired examination can be performed.

The specimens obtained were examined within one or two hours after aspiration. The quantity and appearance of the fluid, in regard to color and clearness, then the reaction, whether neutral, alkaline or acid, and the figure of alkalinity or acidity, were ascertained. For the reaction, blue and red litmus paper was used, while the degree of alkalinity was determined by titration, with methyl-orange and $\frac{1}{10}$ standard solution of hydrochloric acid. The ferments (amylpsin, steapsin and trypsin) were estimated by

employing agar tubes² and gauging the amounts by the digested piece of the agar column, stated in millimeters. I am greatly obliged to Dr. O. Hensel for having examined seven specimens from my cases.

Altogether, I have examined the duodenal contents of thirty-two people with the fractional method. In all the bouillon test meal was used; in most of the patients the duodenal contents were also examined in the fasting condition. It will be best to first give the results of these examinations in table form.

REMARKS. The table on pages 820-826 begins with two apparently normal individuals (Group I). In Case 1, R. M., the alkalinity of the duodenal contents in the fasting condition is 30 while one-half hour after the bouillon test meal it is only 10, then it goes to 25, 25 and ultimately to 30. The ferments, likewise, are strongest in the fasting condition while they are weakest one-half hour after the test meal, to increase in strength later on.

Case 2, also belonging to the apparently normal, shows already a different relation. Here the alkalinity in the fasting condition is 20; half an hour after the test meal it is the same. The ferments in the fasting condition are weaker than half an hour after the bouillon; one hour after the test meal they are strongest while later the steapsin ferment grows weaker.

Group II. Five cases with normal gastric secretion, HCl+, acidity 60. In A. M., R. S. and J. M. W. the alkalinity increases up to the end of the first hour, it then slightly diminishes. In Mrs. T. T. and W. B. the alkalinity shows a steady increase up to the end of the two hours.

The ferments show great variations, but, on the whole, their strength, on an average, is greatest about one hour after the bouillon test meal.

Group III. Eleven cases of hyperchlorhydria, in three of which the fasting duodenal contents were examined, show in two a slightly diminished alkalinity one-half hour after the bouillon test meal, while in one there was apparently no difference.

The figures of the alkalinity fluctuated between 5 and 40 and were usually highest between one hour and one and a half hours after the bouillon test meal. The ferments, likewise, showed, in a general way, the same peculiarity, being strongest about that time.

Group IV comprises 4 cases of subacidity and 1 of cholelithiasis, with unknown gastric secretion. The degree of alkalinity fluctuated between 10 and 35; once it was 70 and once in the same patient, with the biliary fistula, it was found to be acid or -10. The strength of the ferments was usually highest between one and a half hours after the bouillon test meal.

² Einhorn, Max: Agar Tubes for the Estimation of the Pancreatic Ferments, Med. Record, January 15, 1910; also Recent Studies of Pancreatic Secretions, Med. Record, January 12, 1915.

4	Miss R. S.	Nervous regurgitation	HCl+; ac., 60	Feb. 5, 1918 ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	6 c.c.; yellow 6 c.c.; yellow 2 c.c.; yellow 1½ c.c.; yellow	5 15 10 10	0 4½ 6 0	½ 1½ 1½ 1	Tr. Tr. Tr. Tr.
5	Mr. J. M. W.	Duodenal ulcer	HCl+; ac., 60	Oct. 30, 1917 ½ h. a. b. 1 h. a. b. (boiled) 1 h. a. b. 1½ h. a. b. 2 h. a. b.	Yellow; cloudy Yellow; cloudy Watery; yellow Light; yellow Light; yellow	40 40 50 40 40	5 0 6 10 8	½ 0 2 6 5 4	Tr. 0 2 5 5 4
6	Mr. T. T.	Gastric ulcer	HCl+; ac., 60	Oct. 27, 1917 ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	Cloudy Clear Clear Turbid	10 10 15 25	0 Tr. 2 5 6 2	Tr. Tr. 2 5 6 Tr.	Tr. Tr. 2 2 Tr. Tr.
7	Mrs. W. B.	Gastric ulcer	½ h. a. b., HCl+; ac., 40 1 h. a. b., HCl+; ac., 60	Mar. 9, 1918 ½ h. a. b. 1 h. a. b.	4 c.c.; yellowish-green tinge; turbid 1 c.c.; yellow; slightly turbid ½ c.c.; yellow; slightly turbid	15 20 25	8 8 7½	2 3 7	4 3½ 4
8	Mrs. J. T. P.	Cholecystitis; gastric ulcer	HCl+; ac., 65	Feb. 10, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b.	7½ c.c.; yellow; turbid 7 c.c.; yellow; turbid 5½ c.c.; yellow; turbid 5 c.c.; reddish tinge; sediment	40 20 35 40	20 12 6 5½	7 3 2½ 1	4½ 2 4 4
9	Mr. C.	Duodenal ulcer	HCl+; ac., 70	Sept. 17, 1917 ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	8 c.c.; light yellow; sediment 6 c.c.; golden yellow 7 c.c.; golden yellow 2 c.c.; golden yellow 4½ c.c.; golden dark	40 15 20 25 30	15 6 6 5 6	1 1½ 3 1 5	5 1½ 4 2 5

h. a. b. = hour(s) after bouillon.

TABLE OF CASES IN WHICH FRACTIONAL EXAMINATIONS OF THE DUODENAL CONTENTS WERE MADE—continued.

No.	Name.	Diagnosis.	Gastric contents.	Date and time.	Duodenal contents.					Remarks.
					Quantity and appearance.	Alkalinity.	Amylopsin.	Steapsin.	Trypsin.	
10	Mr. P. D.	Duodenal ulcer	HCl +; ac., 72	—Continued Sept. 30, 1918 1/2 h. a. b. 1 h. a. b. 1 1/2 h. a. b.	Pale green Yellow, green Green	17 1/2 22 1/2 10	8 9 6	1/2 1 1 1/2	1 1 1/2 1 1/2	
11	Mrs. L. M.	Enteroptosis; hy- perchlorhydria	HCl +; ac., 80	Mar. 17, 1918 Fasting 1 h. a. b. 1 h. a. b. 1 h. a. b.	1 c.c.; green; turbid 5 c.c.; greenish yellow; clear	20 30	8 7	4 3 3	5 3 3	
12	Mrs. E. W. G.	Gastric ulcer	HCl +; ac., 80	Nov. 21, 1917 1/2 h. a. b. 1 h. a. b. 1 1/2 h. a. b. 2 h. a. b.	1 c.c.; yellow, tinge of green; clear 2 c.c.; yellow, tinge of green; clear 2 c.c.; yellowish green; slightly turbid	30 25	8 8	1 2 2	6 6 6	
13	Mr. W. E.	Gastric ulcer; nephrolithiasis	HCl +; ac., 80	Sept. 27, 1917 1/2 h. a. b. 1 h. a. b. 1 1/2 h. a. b. 2 h. a. b.	Turbid Turbid Green; turbid Green; turbid	0 10 12 1/2 12 1/2	0 5 6 5	0 1 1 1/2 1	0 0 2 1	
14	Mr. I. O.	Gastric ulcer	HCl +; ac., 90	Oct. 4, 1917 1/2 h. a. b. 1 h. a. b. 1 1/2 h. a. b. 2 h. a. b.	Colorless; clear Yellow; turbid Green; turbid Green; turbid	0 15 10	0 8 10	0 0 1/2	0 1 1	
15	Mr. M. S.	Gastric ulcer	HCl +; ac., 90	Jan. 18, 1918 1/2 h. a. b. 1 h. a. b. 1 1/2 h. a. b. 2 h. a. b.	2 c.c. gold yellow 4 c.c. gold yellow; clear 3 c.c. gold yellow; clear 2 c.c. gold yellow; clear	10 20 20 10	2 1/2 5 5 7	1 2 2 2	3 3 3 2	

16	Mr. W. F. Mc.	Duodenal ulcer	HCl +; acidity, 90	Sept. 19, 1918 ½ h. a. b. 1 h. a. b.	Yellow Colorless Colorless Colorless	20 25	4 3 3½ 3	1 1 ½ 2	5	
17	Mr. C. M. D.	Duodenal ulcer	HCl +; ac., 90	Feb. 28, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	½ c.c.; whitish; turbid 1 c.c.; turbid; yellowish tinge 1 c.c.; slightly yellow; turbid 3 c.c.; yellowish-green tinge; slightly turbid 4 c.c.; yellowish green 20 30	0 9 5 8 11	Tr. 1½ 4 4 1½	Tr. 2 2½ 5 8	
18	Mrs. H. M. R.	Pyloric ulcer	HCl +; ac., 96	Feb. 9, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	4 c.c.; yellow; turbid 5 c.c.; yellow; turbid 2 c.c.; yellow; turbid 1½ c.c.; yellow; turbid 3½ c.c.; yellow; turbid	20 15 20 30 30	6½ 5½ 9 6½ 6½	5½ 2½ 6 2 2½	3 2½ 3 4 2	
				Group IV.						
19	Mr. J. D.	Duodenal ulcer	HCl +; acidity 35	Mar. 12, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	6 c.c.; yellow; turbid 4 c.c.; yellow; turbid; greenish tinge 6 c.c.; straw colored; very slightly turbid 2 c.c.; yellow; very slightly turbid 3 c.c.; yellow; very slightly turbid	35 30 35 30 30	5 10 9 6 7	1 2 2½ 1 1½	4 4½ 4 2 5	
20	Mr. M. S.	Probable cholelithiasis; chronic gastric catarrh	HCl +; ac., 35	Feb. 23, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	6 c.c.; yellow, green; turbid 6 c.c.; yellow, green; turbid ½ c.c.; straw yellow ¼ c.c.; yellow; clear ¼ c.c.; yellow	15 20	8 14 10 6 Tr.	1½ 7 4 1 Tr.	Tr. Tr. 4 1 1 Tr.	

h. a. b. = hour(s) after bouillon.

Urobilinogen
not present.

TABLE OF CASES IN WHICH FRACTIONAL EXAMINATIONS OF THE DUODENAL CONTENTS WERE MADE—*continued*.

No.	Name.	Diagnosis.	Gastric contents.	Date and time.	Duodenal contents.					Remarks.	
					Quantity and appearance.	Alkalinity.	Amylopsin.	Steapsin.	Trypsin.		
					GROUP IV—Continued						
21	Dr. F. W. H.	Gastric catarrh	HCl?; ac., 20	Mar. 10, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	15 c.c.; greenish;turbid 10 c.c.; turbid; greenish tinge 6 c.c.; yellow; clear 4 c.c.; yellow; clear 6 c.c.; straw yellow; slightly turbid	Ac. Ac.	0 0	0 0	0 0	0 0	Probably from the stomach.
22	Mrs. W.	Cholelithiasis	Mar. 23, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	8 c.c.; golden yellow; very slight turbidity 8 c.c.; straw yellow; very slight turbidity 10 c.c.; light yellow; turbid 6 c.c.; yellow; greenish tinge; clear 7 c.c.; yellow; clear; greenish tinge	10 12 12 10 12	11 9 8 13 3	3 2 3 6 4	3 6 6 5 4	5½ 6 6 5 4	
23	Mrs. A. L. M.	Biliary obstruction and fistula	HCl +; ac., 40	Feb. 19, 1918 Fasting ½ h. a. b. 1 h. a. b. 1½ h. a. b. 2 h. a. b.	1 c.c.; yellow; turbid 2 c.c.; yellow; turbid 3 c.c.; yellow; turbid 6 c.c.; clear 7 c.c.; yellow; turbid	15 20 20	5 5 7	Tr. 1½ 1½	Tr. 1 Tr.	Tr. 1 Tr.	Pancreatic rennet +. Free acid present.
					GROUP V.						
24	Mr. J. M. M.	Achylia gastrica; probable cholelithiasis	HCl, 0; neutral	Feb. 23, 1918 Fasting ½ h. a. b.	2 c.c.; yellowish green; slight turbidity 6 c.c.; brownish yellow; very slightly turbid	20 30	6 17	Tr. 8	Tr. 10	1 10	

25	Mr. S. E.	Chronic myelitis; achylia gastrica	HCl, 0; ac., 0	1 h. a. b.	1½ c.c.; yellow; very slightly turbid	20	5	2	1½	Urobiligen not present.	
				1½ h. a. b.	2 c.c.; yellow; slightly turbid	40	11	Tr.	2		
				2 h. a. b.	2 c.c.; very slightly turbid	30	8	1	1		
				Mar. 24, 1918							
				Fasting	10 c.c.; yellow; turbid	35	12	1	5		
				½ h. a. b.	10 c.c.; yellow; greenish tinge; turbid	30	14	1	5		
				1 h. a. b.	½ c.c.; straw yellow; slightly turbid	20	9	3	6		
				1½ h. a. b.	1 c.c.; golden yellow; clear	25	11	2	4		
26	Mr. A. A. C.	Carcinoma of the stomach	HCl, 0; ac., 25	Mar. 8, 1918	4½ c.c.; milky; turbid	50	8	2	Tr.		
				Fasting	6 c.c.; yellow; turbid; sediment	55	11	6	4		
				1 h. a. b.	6 c.c.; light yellow; turbid; greenish sediment	60	10	5	6		
				1½ h. a. b.	5 c.c.; greenish yellow and sediment	60	10	3	4		
				2 h. a. b.	1 c.c.; greenish yellow and sediment	60	9	Tr.	3		
				GROUP VI.							
27	Mr. O. H.	Diabetes mellitus; thrombo-angitis obliterans	Jan. 12, 1918	Yellow; clear	20	6	12	2		
				½ h. a. b.	Yellow; clear	24	10	5	3		
				1 h. a. b.	Yellow; clear	10	12	5	6		
				2 h. a. b.	Yellow; clear	20	6	1	2		
28	Mr. C.	Thrombo-angitis obliterans	Mar. 15, 1918	4 c.c.; yellow; turbid	15	6	1	2		
				Fasting	½ c.c.; yellow; turbid	7	0	3			
				½ h. a. b.	5 c.c.; greenish-yellow; turbid	20	14	5	3		
				1 h. a. b.	1 c.c.; yellow; greenish; slight turbidity	30	8	2	4		
				2 h. a. b.	½ c.c.; yellow	..	8	0	3		

h. a. b. = hour(s) after bouillon.

TABLE OF CASES IN WHICH FRACTIONAL EXAMINATIONS OF THE DUODENAL CONTENTS WERE MADE—continued.

No.	Name.	Diagnosis.	Gastric contents.	Date and time.	Duodenal contents.					Remarks.						
					Quantity and appearance.	Alkalinity.	Amylopsin.	Steapsin.	Trypsin.							
29	Mr. S.	Thrombo-angitis	—Continued Jan. 31, 1918 Fasting	3 c.c.; watery; clear	..	0	0	0							
					2 c.c.; yellowish	..	4	2	0							
					1 h. a. b.	N.	2	3	0		Remnet +.					
					1 h. a. b.	..	0	0	0							
					1 1/2 h. a. b.	..	0	0	0							
30	Mr. B.	Thrombo-angitis obliterans	Jan. 29, 1918 1/2 h. a. b.	6 c.c.; yellow; slightly turbid	25	5	1 1/2	0							
					3 c.c.; yellow; green;	20	10	2	4							
					8 c.c.; gold; yellow;	25	5	1	2							
					turbid	15	6	1	2							
					3 c.c.; yellowish green;	15	6	1	2							
31	Mr. M.	Thrombo-angitis obliterans	Jan. 30, 1918 Fasting	1/2 c.c.; yellow; clear	Alk	0	1/2	1							
					3 c.c.; yellow; clear	10	0	Tr.	Tr.							
					3 c.c.; yellow; clear	10	0	0	0							
					8 c.c.; yellow; clear	20	0	1/2	1/2							
					3 c.c.; yellow; clear	-5	0	1/2	1/2							
					32	Mr. K.	Thrombo-angitis obliterans	Mar. 27, 1918 Fasting	8 c.c.; whitish; turbid;	5	6	8	1		
										no bile						
										10 c.c.; yellow; green- ish; turbid	55	11	5	6		
										3 c.c.; light yellow;	15	9	1	4		
										turbid	15	9	5	1		
5 c.c.; whitish; turbid;	15	9	5	1												
no bile																
7 c.c.; whitish; turbid;	20	7	2	2												
no bile																

h. a. b. = hour(s) after bouillon.

Group V comprises 3 cases of achylia, 2 benign and 1 complicated with cancer of the stomach. The alkalinity fluctuates between 20 and 40 in the 2 benign cases and between 50 and 60 in the cancer case. The strength of the ferments is highest between half an hour and one hour after the bouillon test meal.

Group VI. Six cases of thrombo-angiitis obliterans, one of which was complicated with diabetes mellitus, were likewise examined. They were all patients of Dr. Willy Meyer and were treated by duodenal instillation of Ringer's solution. I am greatly indebted to Dr. Willy Meyer for permission to examine their pancreatic function. The alkalinity was, on an average, somewhat lower than normal, fluctuating between 10 and 24; once it was 5 and once 55.

In 3 of the 6 cases the ferment activity was at times greatly reduced (Cohen, Scherr, Metloff), the steapsin ferment showing the greatest variations.

EPICRISIS. The grouping of the table was arranged according to gastric secretion in order to see whether the latter has any bearing on the alkalinity curve. *A priori*, one would expect a lowered alkalinity in cases of hyperchlorhydria and conversely an increased alkalinity in cases of subacidity. This seems to be true in a certain measure, but not constantly so. It seems there are other factors besides gastric secretion which play a part in regulating the degree of alkalinity of the duodenal contents. Chief among these are the pancreatic and duodenal juices and the bile. Each one of these is liable to have its own peculiarities and show alterations in disease.

It appeared worth while to look at the different types of alkalinity curves found, regardless of gastric juice or any disease present.

The accompanying types of alkalinity curves can be easily discerned.

Type 1 (Chart I). Decrease of alkalinity during the first half hour after the bouillon, then a steady increase.

Type 2 (Chart III). Increase of alkalinity between one-half and one hour after the bouillon, then slight decrease. Chart II belongs to Type 1, Chart IV belongs to Type 2.

Type 3 (Chart V). Increase of alkalinity during first half-hour after the bouillon, then slight decrease up to one hour, then again increase to one and a half hours, thereupon again a decrease.

Type 4 (Chart VI). There is first a steady increase of alkalinity up to one and a half hours after the bouillon test meal then an abrupt descent of the curve, so that at two hours after the bouillon the contents are acid instead of alkaline.

Of the three ferments each shows its individual peculiarities; the strength of one ferment cannot be gauged by that of the other. It is possible to ascertain the strength of each ferment at the different periods after the test meal and express it in the form of a curve. But each one (A. S. T.) has its own curve.

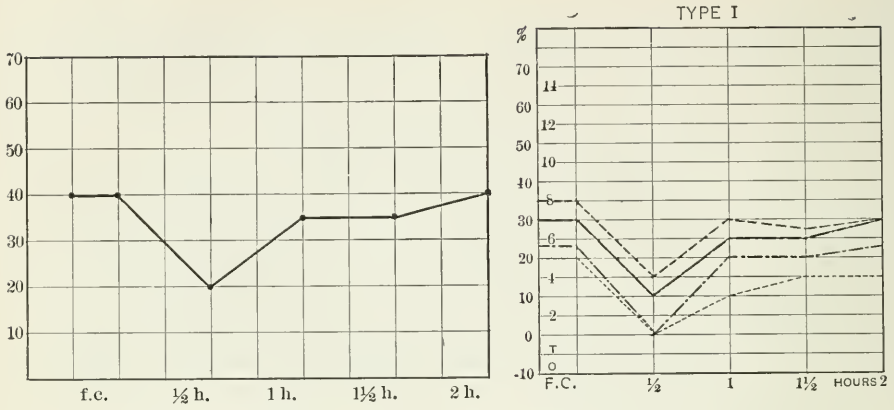


CHART I.—Case of Miss R. M. (No. 1). Alkalinity curve, Type I.

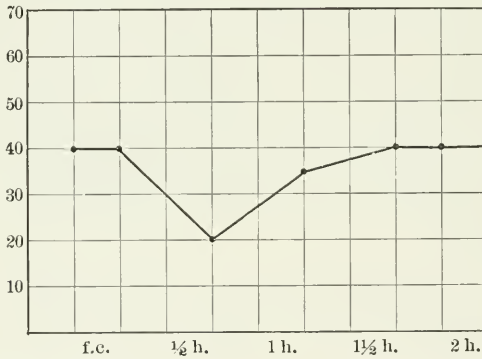


CHART II.—Case of Mrs. J. T. P. (No. 8). Alkalinity curve, Type I.

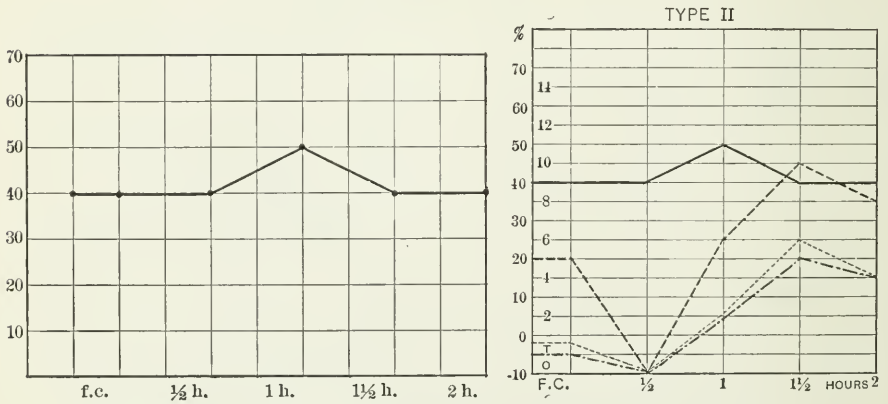


CHART III.—Case of Mr. J. M. W. (No. 5). Alkalinity curve, Type II.

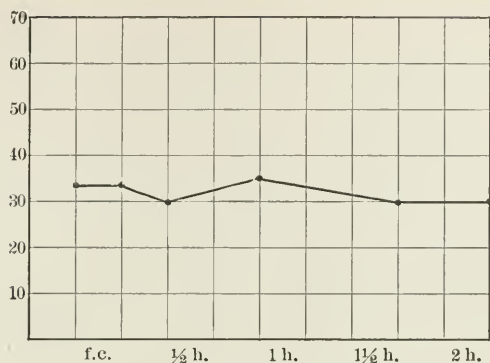


CHART IV.—Case of Mrs. J. D. (No. 19). Alkalinity curve, Type II.

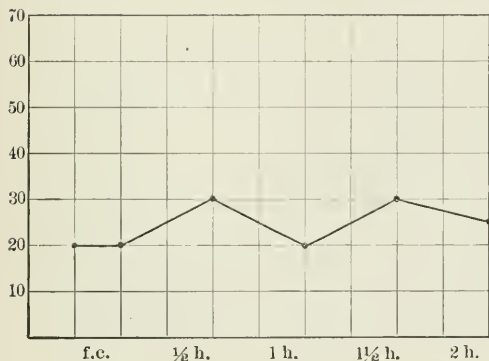


CHART V.—Case of Mrs. L. M. (No. 11). Alkalinity curve, Type III.

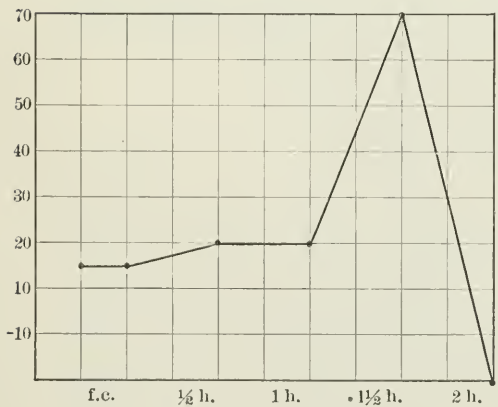
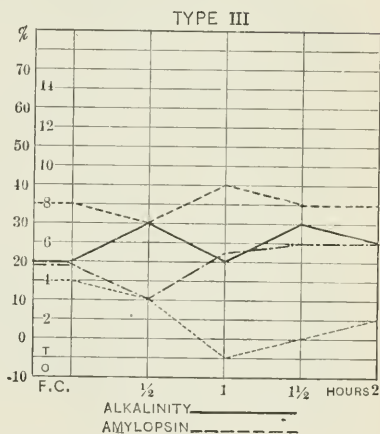
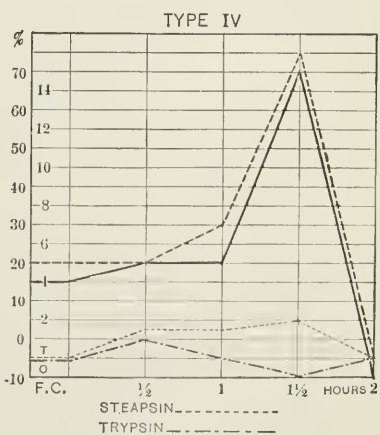


CHART VI.—Case of Mrs. A. L. M. (No. 23). Alkaainity curve, Type IV.



OBJECT OF DETERMINING THE ALKALINITY. The pancreatic secretions act best in an alkaline medium. The reversion of the acid gastric contents into an alkaline mixture is an important function of the duodenum and its neighboring organs.

It can be easily imagined that in pathological conditions this harmonious work in having the right medium will be lacking. We may then have conditions in which the degree of alkalinity is too high, or again too low, *i. e.*, diminished alkalinity or slight acidity.

AT WHAT TIME IS IT BEST TO EXAMINE THE DUODENAL CONTENTS? The fasting duodenal contents usually consist of some pancreatic secretion and bile, perhaps also duodenal secretion. The pancreatic juice this time is generally weak in ferment activity and gastric contents are not admixed therein.

The duodenal contents one to one and a half hours after the bouillon test meal represent a chyle embracing the pancreatic juice at the height of activity, bile, duodenal secretion and an admixture of gastric chyme.

To facilitate the diagnosis of liver and gall-bladder lesions it appears that the examinations in the fasting state will give the best results. For here the investigation of the bile, in as pure a state as we can obtain it, will form the main object.

In pancreatic affections, also in all conditions in which the principal part of the digestive act should be investigated, it will be best to examine the duodenal contents one to one and a half hours after the test meal. The height of the pancreatic activity found at this moment and also the reversion of the admixed gastric chyme from an acid to an alkaline medium, which is a very important function of the duodenum, make this time best suited for the above purposes.

CERTAIN ASPECTS OF THE CLINICAL VALUE OF THE ESTIMATION OF KIDNEY FUNCTION.¹

By EDWARD H. MASON, M.D.,

MONTREAL, CANADA.

(From the Medical Clinic of the Royal Victoria Hospital, Montreal.)

DURING this past year information upon several points in kidney function has accumulated in this clinic, which we believe to be of sufficient interest to warrant its publication. The material upon each of the questions presented is somewhat limited, but we hope that it will be of value to those engaged in similar work.

The necessity of determining kidney function by a combined

¹ This work was made possible by a grant from the James Cooper Fund of McGill University.

series of tests rather than by any single one is an important consideration. Many cases give decidedly deceptive results if a limited number of methods are employed, while too great a mass of information often obscures the essential points. This is well shown in the following case, which is illustrative of findings often encountered when studying nephritis:

Medical No. 28267. Male, aged thirty-four years, admitted to the Royal Victoria Hospital February 14, 1917. Diagnosis: early chronic diffuse nephritis. Complaint: headache. Physical examination was negative, but the urine showed 1 gram of albumin per liter, with a few cellular and granular casts. Blood-pressure: systolic, 135; diastolic, 90. The fundi were normal. Wassermann upon blood and upon cerebrospinal fluid was negative.

NEPHRITIC TEST-MEALS. On February 18 a nephritic test-meal, according to Mosenhal's technic, gave the following:

CHART I.

Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride, Per cent.	Gm.	Nitrogen, Per cent.	Gm.
8 to 10	43	1033				
10 to 12	54	1032				
12 to 2	68	1033				
2 to 4	83	1030				
4 to 6	56	1031				
6 to 8	70	1035				
Total day	374	0.983	3.63	2.097	7.75
Night, 8 to 8	309	1030	0.937	2.81	2.002	6.00
Total, 24 hours	683	6.44	13.75
Intake	1760	8.5	13.4
Balance	+1077	+2.06	-0.35

The meal was repeated on February 26 and on March 8, the latter being done after two weeks of continuous rest and a restricted protein intake.

CHART II.—FEBRUARY 26, 1917.

Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride, Per cent.	Gm.	Nitrogen, Per cent.	Gm.
8 to 10	86	1023				
10 to 12	102	1024				
12 to 2	200	1014				
2 to 4	245	1014				
4 to 6	125	1022				
6 to 8	100	1025				
Total day	868	0.90	7.74	0.747	6.42
Night, 8 to 8	590	1022	1.21	7.14	0.834	4.92
Total, 24 hours	1458	14.88	11.34
Intake	1760	8.5	13.4
Balance	+302	-6.38	+2.06

CHART III.—MARCH 8, 1917.

Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride. Per cent.	Gm.	Nitrogen, Per cent.	Gm.
8 to 10	45	1032				
10 to 12	60	1032				
12 to 2	100	1026				
2 to 4	102	1027				
4 to 6	100	1022				
6 to 8	94	1022				
Total day	501	1.38	6.90	1.174	5.87
Night, 8 to 8	370	1027	1.22	4.51	1.262	4.67
Total, 24 hours	871	11.41	10.54
Intake	1760	8.5	13.4
Balance	+889	-2.91	+2.86

From a consideration of the above three meals one would think that on February 18 there was a moderate degree of passive congestion of the kidneys. On February 26 there was no evidence of passive congestion but the findings indicated a nephritis, as shown by a slightly increased night urine and an inability to properly concentrate nitrogen at night. On March 8 the results more closely resembled the findings on February 18. The above three test-meals alone present a very inaccurate idea of the true kidney state, but when they are considered in connection with further findings much light is thrown upon the condition. Three estimations of the rate of urea and chloride excretion follow:

Further, the phthalein on two occasions showed:

Date.	First hour.	Second hour.	Total.
February 23, 1917	82	15	97
March 1, 1917	68	27	95

Now the whole aspect of the case is changed, there being definite evidence of a hyperactive organ, as shown by an increased rate of urea excretion, a raised chloride threshold and an excessively high phthalein output, especially during the first hour. On March 12, after treatment, both the urea and chloride functions show marked improvement. The case would therefore be classified as a chronic diffuse nephritis. Lewis,² in his recent article, clearly showed the period of hyperactivity through which such kidneys passed before progressing into a degenerating nephritis, where the functions are grossly impaired. Such findings have been rather common with us and I think emphasize the importance of a thorough functional examination, especially for kidneys in the early stages of disease.

PRIMARY HYPERTENSION. In primary hypertension we have an obscure symptom-complex which some believe to be a disease entity while others consider it to be primarily a kidney condition. Lewis recently published results showing the abnormally high rates of urea excretion usually present, explaining them as due to a stage of

² Arch. Int. Med., 1915, xvi, 733.

CHART IV.

Date.	Weight. kilos.	Urine per 24 hours. c.c.	Urea.				Sodium chloride.				Thres- hold.		
			Gm. per liter of blood. Ur.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	McLean's index.	Ambard. K.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	Gm. per liter of plasma.			
										Calcu- lated.		Actual.	Differ- ence.
Feb. 23, 1917	59.3	1272	0.180	20.73	26.35	559	0.033	9.87	12.55	6.015	6.718	+0.703	6.323
Feb. 27, 1917	59.1	2448	0.120	9.66	23.64	774	0.028	6.30	15.42	6.013	6.406	+0.393	6.013
Mar. 12, 1917	59.2	888	0.225	21.96	19.48	272	0.048	9.80	8.70	5.950	6.281	+0.331	5.951

CHART V.

Medical No.	Date.	Weight. kilos.	Urine per 24 hours. c.c.	Urea.				Sodium chloride.				Thres- hold.		
				Gm. per liter of blood. Ur.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	McLean's index.	Ambard. K.	Gm. per liter of urine. C.	Gm. per 24 hours. D.	Gm. per liter of plasma.			
											Calcu- lated.		Actual.	Differ- ence.
25077	Jan. 29, 1917	36.4	4128	0.150	2.44	10.05	172	0.057	3.70	15.26	6.067	6.625	+0.558	6.188
24839	Nov. 24, 1916	64.8	1512	0.330	15.73	23.73	120	0.070	6.35	9.60	5.918	6.312	+0.394	6.014
24827	Nov. 25, 1916	56.2	8232	0.270	1.80	14.81	44	0.121	1.30	10.70	5.846	6.500	+0.654	6.274

CHART VIII.

Serial No.	Medical No.	Date.	Weight, kilos.	Urine per 24 hours, c.c.	Urea.			Sodium chloride.				Thresh-hold.		
					Gm. per liter of urine, C.	Gm. per 24 hours, D.	McLean's index.	Ambard. K.	Gm. per liter of urine, C.	Gm. per 24 hours, D.	Calculated.		Actual.	Difference.
I	25224	Feb. 8, 1917	60.0	2280	6.81	15.53	55.5	0.110	1.68	3.81	5.759	5.75	-0.009	5.611
II	25337	Mar. 12, 1917	61.8	1944	17.77	34.53	171.0	0.061	18.15	35.28	6.376	6.125	-0.251	5.369
III	25496	Mar. 8, 1917	60.8	2712	12.48	33.84	178.0	0.060	3.30	8.94	5.871	5.812	-0.059	5.061
IV	25498	May 22, 1917	53.4	2856	5.53	15.79	141.0	0.067	2.30	6.56	5.830	5.687	-0.143	5.477
V	24780	Nov. 11, 1916	59.1	2880	4.86	13.99	95.0	0.083	6.30	15.26	5.994	5.500	-0.494	5.126
	25389	Nov. 21, 1916	58.1	2232	14.55	10.12	48.5	0.115	3.80	14.06	6.000	5.906	-0.094	5.526
		Mar. 14, 1917	60.0	696	19.11	30.96	387.0	0.041	10.00	16.32	5.762	6.312	+0.613	6.233
VI	25266	Apr. 11, 1917	57.9	3312	19.11	30.96	387.0	0.041	10.00	16.32	5.762	6.312	+0.613	6.084
VII	25492	Apr. 4, 1917	62.0	1632	0.225	0.225	0.225	0.225	5.3	19.44	6.004	5.812	-0.192	5.618
VIII	24895	Jan. 19, 1917	20.9	9408	0.225	0.225	0.225	0.225	5.4	50.8	6.776	6.750	-0.026	5.428
IX	25410	Apr. 11, 1917	51.6	4752	0.225	0.225	0.225	0.225	1.6	7.60	5.830	5.937	+0.107	5.725
X	24632	Nov. 29, 1916	46.0	5040	5.98	30.16	139.0	0.068	3.8	19.15	6.039	5.937	-0.102	5.518
XI	25410	Mar. 14, 1917	68.8	1272	14.02	17.83	88.0	0.085	3.3	12.07	5.966	6.156	+0.190	5.810
XII	25121	Feb. 15, 1917	56.1	4824	5.05	24.35	198.0	0.056	4.0	19.29	6.023	6.875	+0.852	5.900
XIII	25226	Feb. 15, 1917	85.5	1272	25.41	32.30	97.0	0.081	8.6	10.94	5.918	6.812	+0.894	6.514

CHART IX. MEDICAL NO. 24778.

Date.	Weight, kilos.	Urine per 24 hours, c.c.	Urea.			Sodium chloride.				Thresh-hold.		
			Gm. per liter of urine, C.	Gm. per 24 hours, D.	McLean's index.	Ambard. K.	Gm. per liter of urine, C.	Gm. per 24 hours, D.	Calculated.		Actual.	Difference.
Nov. 6, 1916	55.8	1440	6.3	9.07	33.5	0.113	3.16	4.53	5.805	6.493	+0.688	6.308
Nov. 20, 1916	58.2	3888	3.61	14.04	50.0	0.196	4.37	16.99	5.806	6.312	+0.506	5.956
Dec. 2, 1916	56.8	1608	2.85	4.56	16.6	0.196	3.0	4.82	5.806	6.687	+0.881	6.501
Dec. 12, 1916	55.2	3933	4.6	18.09	41.0	0.125	3.04	11.95	5.918	6.812	+0.894	6.414

irritability or increased tissue metabolism. Such findings are also present in exophthalmic goitre and fever and may be expected whenever there is a raised basal metabolism. The following 3 cases of hypertention confirm the results of Lewis, also presenting data upon the chloride threshold:

The impaired rate of urea excretion in the third case may be explained by the fact that the prolonged hyperactivity has led to a state of true degenerative nephritis.

As an example of an advanced grade of degenerative nephritis that may develop secondary to prolonged hyperactivity due to hyperthyroidism the following case is instructive:

CHART VI.—MEDICAL NO. 24776, FEBRUARY 8, 1917.

NEPHRITIC TEST-MEAL.						
Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride, Per cent.	Gm.	Nitrogen, Per cent.	Gm.
8 to 10	182	1012				
10 to 12	74	1016				
12 to 2	160	1010				
2 to 4	178	1012				
4 to 6	274	1013				
6 to 8	198	1012				
Total day	1066	0.675	7.15	0.278	2.94
Night, 8 to 8	740	1016	0.618	4.57	0.432	3.19
Total, 24 hours	1806	11.72	6.13
Intake	1940	8.50	13.4
Balance	-134	-3.22	+7.27

LOCAL CONGESTION OF KIDNEYS (ARTERIAL). While studying a series of cases of trinitrotoluol poisoning we obtained functional kidney results which simulate a chronic passive congestion, the congestion probably being of arterial origin, as Odland³ has shown that trinitrotoluol acts mainly upon the smaller arterial walls, causing their degeneration, with a resultant perivascular edema. A test-meal in such a case follows:

CHART VII.—MEDICAL NO. 24671, NOVEMBER 22, 1916.

NEPHRITIC TEST-MEAL.						
Time of day.	Urine, c.c.	Specific gravity.	Sodium chloride, Per cent.	Gm.	Nitrogen, Per cent.	Gm.
8 to 10	95	1029				
10 to 12	48	1029				
12 to 2	60	1030				
2 to 4	55	1030				
4 to 6	38	1030				
6 to 8	65	1030				
Total day	361	0.43	1.55	1.71	6.19
Night, 8 to 8	260	1028	0.44	1.14	1.59	4.15
Total, 24 hours	621	2.69	10.34
Intake	1760	8.5	13.4
Balance	+1139	+5.81	+3.06

³ Arch. Int. Med., 1817, xix, 1.

THE CHLORIDE THRESHOLD IN DIABETES MELLITUS. It is generally stated that the level of the chloride threshold is lowered in diabetes mellitus. This point was determined in 13 cases. It would seem that the level of the threshold is often found to change at different times in the course of the disease. We do not understand upon what factors this varying threshold depends, as shown in Cases V and IX. Whether the raising of the threshold indicates a progressive nephritis we are not prepared to state.

Chart VIII represents the rate of urea and of chloride excretion in 13 cases of diabetes mellitus.

ACTION OF DIGITALIS UPON THE CHLORIDE THRESHOLD. Whether digitalis is of any therapeutic value in lowering the chloride threshold depends upon the type of case. In conditions of truly advanced nephritis, with edema and raised thresholds, there is a response to its administration, probably favoring, to a certain extent, the elimination of chlorides. But with the discontinuance of the drug the threshold promptly returned to its former if not a higher level. At best it is only a temporary measure. In cardiorenal disturbances, especially when the condition is mainly cardiac, with a markedly raised threshold, the response is prompt, undoubtedly relieving the cardiac strain by emptying the blood plasma of accumulated chlorides and secondarily of fluid. Its action in chronic diffuse nephritis is well shown in the following case:⁴

Admitted to the Royal Victoria Hospital November 4, 1916. Diagnosis: chronic diffuse nephritis. Digitalis started on November 8, 15 minims of tincture per day. On November 10, 30 minims per day; November 20, 45 minims per day. Discharged November 28.

In cardiorenal conditions the 3 cases presented in Chart X are typical. The first two represent findings in purely cardiac cases, while the third one (Medical No. 24849) is a mixed case, there being considerable evidence of nephritis, as shown by the impaired rate of urea excretion. The first case (Medical No. 25100) on February 26, 1917, had been receiving 45 minims of tincture of digitalis for four weeks. The drug was stopped on March 2, with a resulting rise in the level of the chloride threshold. On May 4 the case was readmitted (Medical No. 25711) and was put upon 30 minims of tincture of digitalis, which was continued until after the second estimation on May 25, 1917.

The second case (Medical No. 25030) had received 45 minims of tincture of digitalis per day for five days previous to the first estimation. The drug was discontinued on January 10, 1917. Re-admitted February 22 (Medical No. 25308). He received 30 minims of the tincture every day during the period which the three estimations cover.

The third case (Medical No. 24849) received 30 minims of tincture of digitalis from December 3 to 9 inclusive.

⁴Scientific Reports, Royal Victoria Hospital Series B, No. 1, 203.

CHART X.

Medical No.	Date.	Weight, kilos.	Urine per 24 hours, c.c.	Urea.			Sodium chloride.				Thresh-hold.			
				Gm. per liter of blood, Ur.	Gm. per liter of urine, C.	Gm. per 24 hours, D.	Gm. per 24 hours, D.	Gm. per liter of plasma.	Calculated.	Actual.		Difference.		
25100	Feb. 26, 1917	46.7	2400	0.240	8.16	19.64	188.0	0.058	6.0	14.40	6.043	5.437	-0.606	5.014
	Mar. 8, 1917	49.6	1488	0.225	12.34	18.36	229.0	0.053	10.8	16.07	6.120	5.937	-0.183	5.437
	Mar. 15, 1917	50.2	1968	0.270	9.58	18.84	143.0	0.067	3.3	6.48	5.855	5.750	-0.105	5.515
25711	May 9, 1917	55.6	768	0.435	23.76	18.24	76.0	0.092	0.3	0.33	5.629	5.250	-0.379	4.871
	May 25, 1917	50.15	1056	0.360	15.67	16.54	90.0	0.084	5.12	5.41	5.870	5.437	-0.433	5.187
25030	Jan. 8, 1917	58.6	2784	0.300	5.85	16.27	67.0	0.098	5.3	15.31	0.000	5.620	-0.380	5.240
	Jan. 15, 1917	55.1	912	0.331	20.82	18.73	126.0	0.071	13.3	12.13	0.055	6.062	+0.007	5.627
	Feb. 7, 1917	65.4	1488	0.450	11.55	17.18	39.4	0.127	0.81	1.20	5.682	6.000	+0.318	5.938
25308	Feb. 26, 1917	58.4	2160	0.210	8.04	17.36	171.0	0.051	8.3	20.08	6.126	6.062	-0.064	5.556
	Mar. 16, 1917	57.3	2400	0.180	6.69	16.05	200.0	0.056	8.9	21.36	6.132	6.125	-0.007	5.613
	Mar. 19, 1917	55.7	1248	0.255	12.07	15.04	130.0	0.070	10.8	13.47	6.054	5.875	-0.179	5.441
24849	Dec. 5, 1916	59.5	1824	0.750	11.16	19.55	17.0	0.196	1.65	3.00	5.743	5.875	+0.132	5.752
	Dec. 11, 1916	61.0	1752	0.705	11.68	17.09	18.6	0.186	2.15	3.77	5.766	6.937	+1.171	6.791
	Dec. 18, 1916	57.5	1461	0.705	11.68	17.09	18.6	0.186	1.85	2.70	5.744	6.000	+0.256	5.876

CONCLUSIONS. 1. The nephritic test-meal to be of the greatest value must be considered in connection with other functional work, preferably the calculation of the rate of excretion of urea and of chlorides and the phthalein test.

2. In primary hypertension the metabolism of the kidney is raised, resulting in an increased rate of urea excretion and a raised chloride threshold.

3. The nephritic test-meal picture in congestion of the kidneys due to an arterial cause closely simulates that due to a venous one.

4. The level of the chloride threshold in diabetes mellitus is usually below the normal of 5.62 gm. per liter. Some cases show a marked tendency for the level of the threshold to become altered at different stages of their condition.

5. As a means of lowering the level of the chloride threshold, digitalis is prompt and efficient in its action, it being most useful when the disturbance is of a cardiac origin.

My thanks are due to Miss Jacobson for her careful work in carrying out a large number of these chemical estimations.

WAR MEDICINE

CONTRIBUTORS

- LIEUTENANT-COLONEL SIMON FLEXNER, M.C., U.S.A. (Director, Rockefeller Institute).
- DR. A. E. TAYLOR, U. S. Food Administration (Prof. of Physiological Chemistry, Univ. of Penna.).
- ASSISTANT SURGEON-GENERAL J. W. TRASK, U.S.P.H.S.
- ASSISTANT SURGEON-GENERAL W. C. RUCKER, U.S.P.H.S.
- MAJOR RICHARD M. PEARCE, M.C., U.S. A., National Research Council (Prof. of Research Medicine, Univ. of Penna.).
- LIEUTENANT-COLONEL E. G. BRACKETT, M.C., U.S.A.
- MAJOR R. M. YERKES, Sanitary Corps, U.S.A. (Prof. of Psychology, Harvard University).
- SURGEON M. J. ROSENAU, U.S.N.R.F. (Prof. of Preventive Medicine and Hygiene, Harvard Medical School).
- MAJOR R. TAIT MCKENZIE, R.A.M.C. (Prof. of Physical Therapeutics, Univ. of Penna.).
- MR. DOUGLAS C. MCMURTRIE, Director of Red Cross Institute for Crippled and Disabled Men, New York.
- MAJOR E. E. SOUTHWARD, W.S., U.S.A., Director of Psychopathic Department, Boston State Hospital.
- COLONEL WARFIELD T. LONGCOPE, M.C., U.S.A. (Prof. Practice of Medicine, Columbia University).
- DR. DOROTHY REED MENDENHALL, Children's Bureau, U. S. Department of Labor.
- COLONEL FREDERICK F. RUSSELL, M.C., U.S.A.
- DR. C. V. CHAPIN, Superintendent of Health, Providence, R. I.
- DR. GRACE L. MEIGS, Children's Bureau, U. S. Department of Labor.
- MAJOR A. N. RICHARDS, Professor of Pharmacology, Univ. of Penna.
- DR. W. H. F. ADDISON, Assistant Professor of Histology, Univ. of Penna.
- DR. DAVID L. EDSALL, Professor of Clinical Medicine, Harvard Medical School.
- DR. GRAHAM LUSK, Professor of Physiology, Cornell Medical School.
- MAJOR O. H. PERRY PEPPER, M.C., U.S.A., Associate in Medicine, Univ. of Penna.
- DR. W. P. LUCAS, American Red Cross (Professor of Pediatrics, University of California).
- MAJOR FRED H. ALBEE, M.C., Director of Military Reconstruction Hospital No. 3, U.S.A.
- DR. RUFUS COLE, Director Rockefeller Hospital.
- LIEUTENANT W. ESTELL LEE, M.C., U.S.A.
- MAJOR JOHN A. HARTWELL, M.C., U.S.A., Assist. Prof. of Surgery and Prof. Clinical Surgery, Cornell Medical School.
- MAJOR RALPH PEMBERTON, M.C., U.S.A.
- ASSISTANT SURGEON PAUL A. LEWIS, U.S.N.R.F. (Pathologist to Phipps Institute, Philadelphia).

OPEN PNEUMOTHORAX: ITS RELATION TO THE TREATMENT OF EMPYEMA.¹

BY MAJOR EVARTS A. GRAHAM, M.C.,

AND

CAPTAIN RICHARD D. BELL, M.C.,

OF THE EMPYEMA COMMISSION, UNITED STATES ARMY.

INTRODUCTION. In the preliminary report of the Empyema Commission the opinion was given that in the type of cases of empyema which accompanied the prevailing streptococcus pneumonia, operation should not be undertaken early but should be deferred,

¹ This experimental work has been carried out at the Hunterian Laboratory, Johns Hopkins Medical School, through the courtesy of Dr. W. G. MacCallum, to whom we are indebted for many kindnesses.

in order to allow time for the pneumonia to subside and for the empyema to become more localized by the formation of adhesions. One of the principal considerations which led to this opinion was the question of the possible harm to the patient caused by the creation surgically of an open pneumothorax in the presence of an already existing state of severe asphyxia. Notwithstanding the apparently striking clinical confirmation of the soundness of this point of view, as shown by our remarkable reduction in the mortality of 4.3 per cent. as compared with the average mortality of 30.2 per cent. noted in the replies of the various camps to the Surgeon-General's questionnaire of February 21, 1918, it seemed desirable to submit to experimental test some of the considerations which theoretically had led the commission to the adoption of deferred operation. This seemed especially desirable, since there was a possibility that our low mortality might have been due in some measure to a decrease in virulence of the organism. Accordingly, work has been carried out along the following lines: (1) a study of the effects of open pneumothorax in normal and diseased chests, (2) the experimental production of a streptococcus pneumonia and empyema in dogs comparable with that in the human, (3) a study of the effect of early operation in dogs with experimentally produced streptococcus empyema. The limited amount of time available for these investigations prevented as complete a study of the problems as seemed desirable, but nevertheless certain facts have been established which seem to have an important bearing on the method of treating the condition.

PART I.—PNEUMOTHORAX.

Definition. Under normal conditions each pleural cavity is completely filled by its corresponding lung and the cavity of which one speaks is only a potential one. When air is present in a pleural cavity the condition of pneumothorax exists. Air may enter either from an opening through the thoracic wall or from a communication with the lung. If the opening remains patent so that air passes in and out freely the condition is known as an "open pneumothorax." If air is enclosed within a pleural cavity so that its exit is blocked a "closed pneumothorax" is produced. Another type of pneumothorax, commonly called "valve pneumothorax," occurs when air may enter freely but cannot pass out again. The latter type is found usually in connection with communications between the lung and the pleural cavity, especially in tuberculosis and in pulmonary abscess. It is the first type—namely, open pneumothorax—which is of primary interest in this discussion, for it is this condition which is produced by early operation and drainage in cases of empyema. If the pleural infection is not sharply walled off by adhesions the operation will create a pneumothorax, and the insertion of a drainage tube, by continuously allowing the free passage of air into and out of the chest, will maintain an open pneumothorax after the operation.

Importance of Negative Intrapleural Pressure in Maintaining Respiration. By far the most harmful effects, and perhaps the only harmful ones, of a pneumothorax are the changed pressure relationships within the thorax. Normally, each pleural cavity has a potential negative pressure, and it is owing to this negative pressure that respiration can go on. At each inspiration the thoracic cavity is enlarged. This enlargement and the accompanying tendency of the lungs to lag behind obviously makes the pressure still lower within the pleural cavities until after the lungs have been filled with air, expiration occurs and, with the diminution in size of the pleural cavity, the intrapleural pressure tends to approach the atmospheric pressure but does not actually reach that height unless the glottis is closed. These pressures, of course, even normally, are subject to wide variations, depending upon the amplitude of the respiratory movements. They have been measured repeatedly in various ways by numerous observers in human cadavers, in the living human and in animals. Donders,² who was apparently the first to measure them, considered the normal intrapleural tension in man at the end of quiet expiration to be -7.5 mm. Hg. and at the end of inspiration -9 mm. Hg. Aron³ made determinations on a living normal man and found at the height of quiet inspiration an average reading of -4.64 mm. Hg. and at the height of quiet expiration -3.02 mm. Hg. For a more detailed discussion of these points reference may be made to the extensive works of Emerson,⁴ Sauerbruch⁵ and L. Mayer.⁶ It is not within the province of this article to review the literature on pneumothorax exhaustively, since this has been well done by each of the three authors just mentioned. Instead, we shall be concerned here only with those literature references which deal particularly with the salient points of our problem—namely, the relative harmfulness of open pneumothorax.

Prevalent Conceptions of the Mechanics of Open Pneumothorax. In the light of our experiments the prevalent conceptions of open pneumothorax seem to be based on an incorrect understanding of the condition. Practically, without exception, they start from the apparently erroneous assumption that the mediastinal structures constitute an unyielding, almost rigid, partition between the two sides of the thoracic cavity. This assumption in turn has given rise to the idea that one lung is collapsed and that the other lung alone carries on respiration, although somewhat impeded, perhaps, if the opening be a large one, by the bulging of the mediastinum against

² Quoted by Heynsius, Arch. f. d. ges. Physiol., 1882, xxix, 267.

³ Die Mechanik und Therapie des Pneumothorax, 1902, quoted by Emerson, p. 194.

⁴ Pneumothorax, Johns Hopkins Hosp. Rep., 1903, xi, 1.

⁵ Zur Pathologie des offenen Pneumothorax und die Grundlagen meines Verfahrens zu seiner Ausschaltung, Mitteil. a. d. Grenzgeb. d. Med. u. Chir., 1904, xiii, 399.

⁶ Les Bases Physiologiques de la Chirurgie Pleuropulmonaire, Ann. d. l. Soc. Roy. d. Sciences Méd. et Nat. de Bruxelles, 1906, xv, 1.

it. Garré,⁷ for instance, in a series of diagrams to represent the conditions in open pneumothorax, shows the mediastinum as a straight line, in cases in which the opening is small, with one lung collapsed and retracted and the other lung (on the unopened side) of normal size and apparently unaffected. In cases with a large opening he represents essentially the same condition except for a slight bulging of the mediastinum away from and toward the opening on inspiration and expiration respectively. Here, again, the lung on the affected side is shown as contracted into a small mass about the hilum, whereas the opposite lung appears to be relatively unaffected. L. Mayer, after reviewing the literature extensively, states the situation in regard to pressure relationships in open pneumothorax as follows: "On the healthy side the modifications due to the pneumothorax with a small opening ought to adjust themselves by a deviation of the mediastinal pleura, the two surfaces of which are no longer submitted to conditions of identical equilibrium; on inspiration the lowering of intrapulmonary pressure of -7 mm. Hg. not manifesting itself on the fistula side, the mediastinal pleura ought to become curved toward the healthy side and narrow the expansion of the other lung; the inverse should be produced at expiration. In reality these theoretical differences are minimal and are scarcely established by experimentation. If, on the contrary, the pleural opening is widely gaping the atmospheric air enters and goes out freely at each respiratory movement and the lung of this side will not be called upon at all to become distended. At each inspiration the pressure of the two sides of the mediastinal pleura will be different; on the healthy side, negative pressure of 7 mm. Hg., on the other side atmospheric pressure, with aspiration of the mediastinum toward the healthy side, toward which it ought to be markedly convex. In moderate and light expiration the pressure on the two sides remains equal; but if a forced or sudden expiration supervenes the pressure is raised in the normal lung while it remains constant on the incised side, giving a convexity of the mediastinum on the side of the pneumothorax." It is seen, therefore, in Mayer's resumé of the common conceptions regarding the pressure relationships in open pneumothorax that there are several assumptions ordinarily taken for granted: (1) that a marked inequality of pressure exists in the two pleural cavities after the establishment of a communication between one pleural cavity and the external air; (2) that this marked inequality of pressure results in the more or less complete collapse and retraction of the lung on the opened side while the other lung remains but slightly affected; (3) the mobility of the mediastinum is a relatively unimportant factor. These conceptions are so commonly accepted that one finds ingrained in all the literature of pneumothorax references to the "sound lung,"

⁷ Garré's Diagrams are reproduced in L. Mayer's article (loc. cit.). The originals were inaccessible to us.

the "healthy lung," the "unaffected lung," etc., when what is meant is the lung in the unopened pleural cavity, as if it were little, or not all, affected by the opening in the opposite pleural cavity.

Prevalent Conceptions of Open Pneumothorax Seem to be Erroneous in Light of Our Experiments. In our experiments, on the contrary, we have found that normally the mediastinal structures are so mobile that they offer practically no resistance to pressure on either side. In the normal human (both adult and child) the resistance offered by the mediastinum, when one pleural cavity contains air at a known pressure equivalent to that of 10 cm. of water, corresponds to a pressure of only 1 cm. or less of water, which, of course, is practically negligible. For all practical purposes, therefore, from the standpoint of pressure relationships, the thorax may be considered as one cavity instead of two. Any change of pressure in one pleural cavity will affect also the other one almost equally. The common conceptions of collapsed lung on one side and "healthy" or "normal" lung on the other, in the condition of open pneumothorax in the otherwise normal chest, must be erroneous. Roughly speaking, also, the degree of asphyxia which will follow the creation of an open pneumothorax will depend upon (1) the relation of the amount of air entering through the pneumothorax opening to the amount of air permitted to pass down the air-inlet to the lungs, and (2) the ability of the individual to compensate by increasing either the rate or amplitude of his respiratory movements, or both. The dog's mediastinal structures have the same mobility as the human beings; therefore, experimental results obtained on the living dog are applicable to man. The importance of these considerations in regard to the surgical treatment of empyema will be shown later under "General Discussion."

Sehrwald,⁸ as long ago as 1889, arrived at some of the same conclusions which we have drawn from our work. His conclusions, however, seem not to have been based on much experimental work; and, perhaps for that reason, they have not influenced opinion so much as their soundness entitled them to do. For example, he stated that the influence of a unilateral open pneumothorax on respiration depends not on the absolute diameter of the opening but on the relation between the size of this opening and the diameter of the air passage to the lungs. He concluded also that the mobility of the mediastinum was a very important consideration; if it were delicate and easily stretched it would be aspirated so strongly against the "sound" lung that it would hinder its expansion. He made the important statement, furthermore, that very young individuals and those who previously had had normal thoracic organs, because of the delicacy and elasticity of their mediastinum, stand an open pneumothorax with much more difficulty than patients in whom,

⁸ Zum Atmungsmechanismus beim offenen Pneumothorax, Deutsch. med. Wchnschr., 1889, xiv.

because of a strong thickening, the mediastinum has been converted into a firm, unyielding membrane. It is to be noted, however, that even he also had the conception of a "sound lung" as opposed to a collapsed lung, and that he did not recognize that the pressures in the two pleural cavities are practically equal, with the result that both lungs are collapsed to the same extent.

PART II.—EXPERIMENTAL RESULTS.

Parallelism of Thoracic Pressure Relationships in Dog and Human. Experiments have been carried out on both animals and human cadavers. In order to determine whether results obtained on living animals could be considered as applicable to the human, it seemed especially desirable to ascertain, if possible, the comparative mobility of the dog's mediastinum with that of the human under the same pressure relationships, since the dog seemed to be in general the most suitable animal for a study of the living conditions. The experiments which show this comparison will be described first. Since the human experiments could be carried out only on cadavers the procedure chosen was to compare the relationships in the human cadavers with those in recently killed normal dogs and then to compare these results with those obtained by similar means in living dogs. In this manner it was found that the experimental results obtained on living dogs were directly applicable to the living human. The experiments were carried out as follows:

A metal cannula (diameter 4 mm.) was inserted into each pleural cavity (usually in the fifth interspace in about the anterior axillary line). Each cannula was attached by rubber tubing of the same size and kind to a tambour which, by means of an indicator, registered the pressure changes on a smoked drum. In one rubber tube was interposed a T-tube, which was connected in one direction with a water manometer and in the other with a rubber atomizer bulb. By means of the bulb, air was forced into the corresponding pleural cavity until the manometer registered 10 cm. pressure. Simultaneously with the rise of the indicator on the tambour of that side the other indicator also became elevated above its base line. Calibration of the reading of the second indicator showed the equivalent of a pressure of 9 or 9.5 cm. of water. In other words, when a known pressure, equivalent to 10 cm. of water, was established in one pleural cavity there was practically the same pressure in the opposite pleural cavity. This experiment has been carried out on five human cadavers, two of which were infants of four months and fourteen months respectively, one a child, aged fourteen years, and two adults. Duplicate determinations on the same cadaver sometimes showed a variation of 0.5 cm. in the reading of the opposite side, due probably to experimental error: that is, when the pressure of the inflated side was the equivalent of 10 cm. of water,

that of the opposite side registered sometimes only 9 cm. and at other times 9.5 cm. No difference was noted whether the right or left pleural cavity was inflated. These results were strictly comparable with those which were obtained on normal dogs which had been killed with ether. It should be stated, however, that cadavers which had been kept in the refrigerator for several hours showed a difference in pressure sometimes of as much as the equivalent of 3 cm. of water, but control dead dogs kept in the same refrigerator for the same length of time always showed the same variations. Since the objects sought in the experiments was really to determine the extent of mobility of the mediastinum, it was necessary to rule out the possibility of pressure being transferred to the opposite side by being distributed through the diaphragm of the inflated side to the abdomen and from there through the diaphragm of

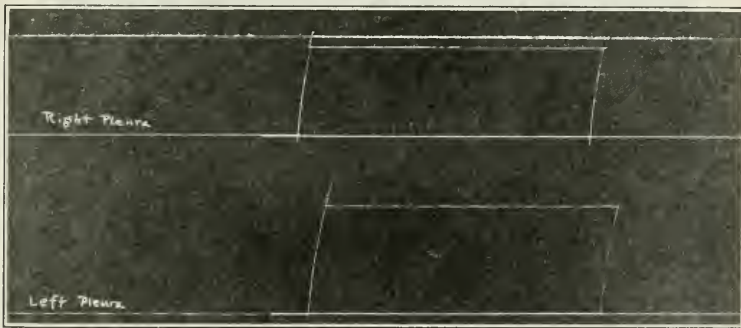


FIG. 1.—Tracing showing that when the left pleural cavity of a fresh adult human cadaver is inflated with air at a pressure of 10 cm. of water the right pleural cavity registers a pressure of 9 cm. The top line is a record of a pressure of 10 cm. made with the tambour attached to the right pleural cavity. Calibration showed that the actual pressure was 9 cm. of water.

the opposite side to that pleural cavity. In order to exclude such a possibility the abdomen was opened by a long median incision before inflation of the pleural cavity. By so doing the transfer of any extra pressure to the opposite pleural cavity by way of the abdomen was obviated. It is clear, therefore, that the distribution of the pressure from one pleural cavity to the other, under the conditions of the experiment, was due to the fact that the mediastinal structures were pushed over against the opposite lung. Furthermore, under a pressure equivalent to 10 cm. of water the rigidity of the mediastinal partition between the pleural cavities in both dogs and the human amounts only to the equivalent of from 0.5 to 1 cm. of water pressure (0.4 to 0.8 mm. of mercury), a value which obviously is practically negligible. (See Figs. 1, 2 and 3.)

It was suggested to us by Dr. Howell that perhaps a more conclusive demonstration of whether or not both lungs are nearly

equally compressed by raising the pressure in one pleural cavity could be made by comparing the relative densities of the two lungs when one pleural cavity was inflated with air at a known pressure. If the pressure relationships in both pleural cavities are affected about equally by altering the pressure in one then both lungs

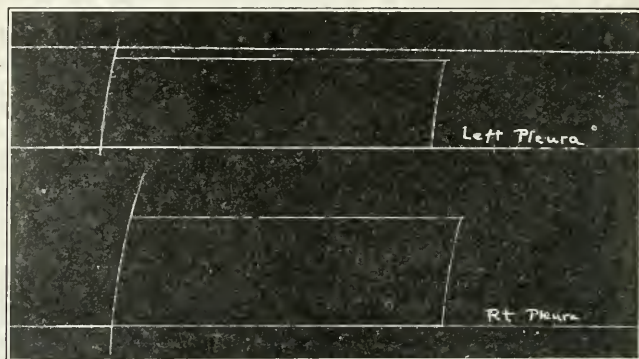


FIG. 2.—A similar tracing with the right pleural cavity inflated. Calibration showed that in this case also there was a difference in pressure of only 1 cm. of water (about 0.8 mm. of mercury).

should be about equally compressed and should show about equal relative densities.

In order to determine this point the following method was used: A normal dog was killed with ether or chloroform and into one pleural cavity air was injected until the pressure was equal to that of

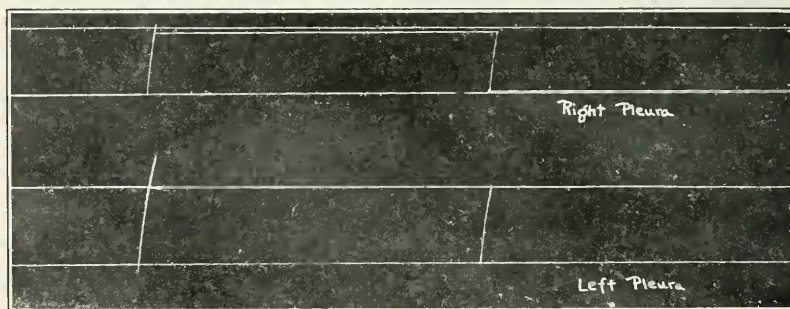


FIG. 3.—Tracing made in the same way with a recently killed dog which shows that the dog is strictly comparable with the human, since here also the difference in pressure between the two pleural cavities amounted to only 1 cm. of water.

10 cm. of water. Through a low tracheotomy in the neck, plaster-of-Paris paste was then pushed down into each main bronchus in order to block its lumen. After allowing the plaster to "set" for a few minutes the lungs were then removed. In this way it was possible to remove the lungs so that they remained in the actual condition

in which they were before the chest was opened. The weight and volume of each lung was then determined, the latter by measuring the amount of water displaced. The plaster was then thoroughly removed from the bronchi and its weight and volume subtracted from that of the corresponding lung. In this manner the specific gravity of each lung was approximately determined, which indicated fairly closely the degree of compression of each lung. When dogs are killed with ether or chloroform the condition of the lungs is not uniform even when nothing else is done to them. One lobe may be well inflated while another is partly collapsed even on the same side. The specific gravity of the two lungs may vary considerably. In some cases the left and in other cases the right lung is the denser. But when the lungs are collapsed by inflating one pleural cavity these variations are not so apparent. The experimental results on five dogs are as follows:

	Density of lungs.	
	Left.	Right.
No. 1. Right pleural cavity inflated with air to a pressure equal to that of 10 cm. of water74	.74
No. 2. Left pleural cavity inflated73	.69
No. 3. Left pleural cavity inflated70	.72
No. 4. Control, not inflated52	.48
No. 5. Control, not inflated43	.51

The results thus demonstrate that the density of one lung practically equals that of the other when one pleural cavity is inflated with air—in other words, there is practically the same amount of compression of both lungs. These results, therefore, furnish additional evidence in favor of the principal conclusion to be drawn by our experimental work—namely, that when the intrathoracic pressure relationships are changed by the creation of an open pneumothorax both lungs are practically equally affected.

Experiments on the Living Dog. Experiments on the living dog not only demonstrate the fact that there is practically an equilibrium of pressure throughout the thorax, as already noted in the recently killed dog and in a fresh human cadaver, but they afforded an opportunity to investigate the extent to which an open pneumothorax produces dyspnea and asphyxia, the mechanism of the attempts at compensation, etc. The method used was in general the same in all the experiments. It consisted essentially in recording simultaneously on a smoked drum the pressure changes in each pleural cavity and in the trachea and the changes in the amplitude and rate of the respiratory movements. To record the variations in pleural pressure the same cannulas as already described above were inserted into the pleural cavities and connected with Marey tambours by means of rubber tubing. The changes of tracheal pressure were recorded in practically the same way by attaching a glass T-tracheal cannula to another tambour, and the variations in the rate and amplitude of the respiratory movements were noted by attaching a fourth tambour to a spring tambour, which was tied to the animal's chest.

When an opening was made into a pleural cavity, therefore, its effects could be at once determined by the movements of the various indicators on the revolving smoked drum. Most of the experiments were conducted under general anesthesia, either urethane or ether, but a few were performed with local cocain anesthesia. No important difference was observed between the changes in pleural pressure produced by the open pneumothorax when an animal was under the influence of general anesthesia and those produced when the opening in the pleural cavity was made under merely local anesthesia with cocain. The factor of general anesthesia, therefore, in most of the experiments can be considered as having no appreciable influence on the results. In the control experiments with cocain no attempt was made to record the tracheal pressure or the changes in the respiratory movements. In all thirty-eight dogs have been used for the work on pneumothorax. In addition, similar experiments have been carried out on three cats and two rabbits. No essential differences were observed regardless of the kind of animal used.

A marked difference in the character of the reaction by the animal occurs, depending upon whether a small or a large opening is made in a pleural cavity. By small or large opening is meant small or large in comparison with the air-inlet to the lungs. Normally the diameter of the air-inlet is the diameter of the opened glottis, but generally in our experiments it was the diameter of the tracheal cannula. A more detailed discussion of the important relationship which exists between the amount of air which enters the lungs and that which enters the pleural cavity will be given later in this article. The characteristic effects produced by a pleural opening smaller than the air-inlet to the lungs may be summarized thus: Immediately upon making the pleural opening there is an increase of pressure in both pleural cavities. Whereas, before making the opening both the inspiratory and expiratory pressures are entirely negative, immediately afterward the pressure rises so much that it is almost entirely positive; the indicators descend below the base line of atmospheric pressure only at about the end of the inspiratory effort. During this time there is noticeable a slight pause early in the course of the expiratory movement just before the pleural pressure reaches that of an atmosphere in its ascent from the negative phase. Simultaneously, also, the tracheal pressure changes in such a way that the indicator practically rests on the base line of atmospheric pressure instead of sweeping above and below the base line on expiration and inspiration respectively. This change is in accord with what is to be expected, since the tracheal pressure is a rough index of the amount of air passing down the trachea into the lungs, and since, obviously, with the pleural pressure almost entirely positive only a small amount of air can pass down the trachea into the lungs.

These changes are also coincidental with an effort on the part

of the respiratory mechanism to compensate by making a greater effort to get air into the lungs; accordingly there is a marked change in the respiratory movement. As a rule, this change is rather an increase in amplitude of respiratory movement than an increase in rate. If the amplitude is increased considerably the rate will of necessity be slower than before. If the pleural opening is small enough to allow compensation, the pleural pressures will gradually diminish so that negative pressure will be reestablished and the tracheal pressure will rise simultaneously as the animal is enabled to get air into its lungs. The negative pressure, however, is never restored so completely as to reach the level at which it was before the opening was made, providing the opening remains in free communication with one pleural cavity. Instead of both the inspiratory and expiratory pleural pressures being negative, as in the normal state, the pressure at the height of expiration will be positive. The ability of the animal, therefore, to withstand an open pneumothorax is dependent upon his ability to compensate by increasing his respiratory effort. Obviously a strong, vigorous animal can compensate better than a weaker one. In our experience young adult dogs have uniformly withstood the harmful effects of an open pneumothorax better than old or weak and emaciated dogs.

It is a very striking fact that usually the restoration of negative pleural pressure can be instantly accomplished by simply closing the pleural opening, thus making a closed instead of an open pneumothorax. But here, again, the intrapleural pressure never becomes so low as it was before the opening was made. Presumably it would become normal as soon as the air contained in the pleural cavity was absorbed; but we have not tested this point. If the opening is made sufficiently large the animal will pass through a state of marked dyspnea and die of asphyxia within a few minutes, owing to his ability to compensate no matter how great his respiratory effort; for if the opening is so large that, despite his maximal respiratory efforts, he is unable to establish a negative pressure in the pleural cavity he will be unable to get air into his lungs, or if he is able to establish a slight negative pressure he may be able to get a little air into his lungs but not enough to maintain life. In this connection it is to be constantly remembered that, roughly speaking, an alteration of pressure in one pleural cavity is accompanied by an alteration of pressure to the same extent in the other pleural cavity. No such condition can be recognized as the collapse of the lung on the affected side and maintenance of respiration with only the other lung, as is the prevalent conception of open pneumothorax. Rather, both lungs must functionate about equally, since practically equal pressures are present in the two pleural cavities. In fact, if the opening into the pleural cavity be made in a favorable place for observation, and if it is not too large to prevent respiratory compensation, the lung on the affected side can

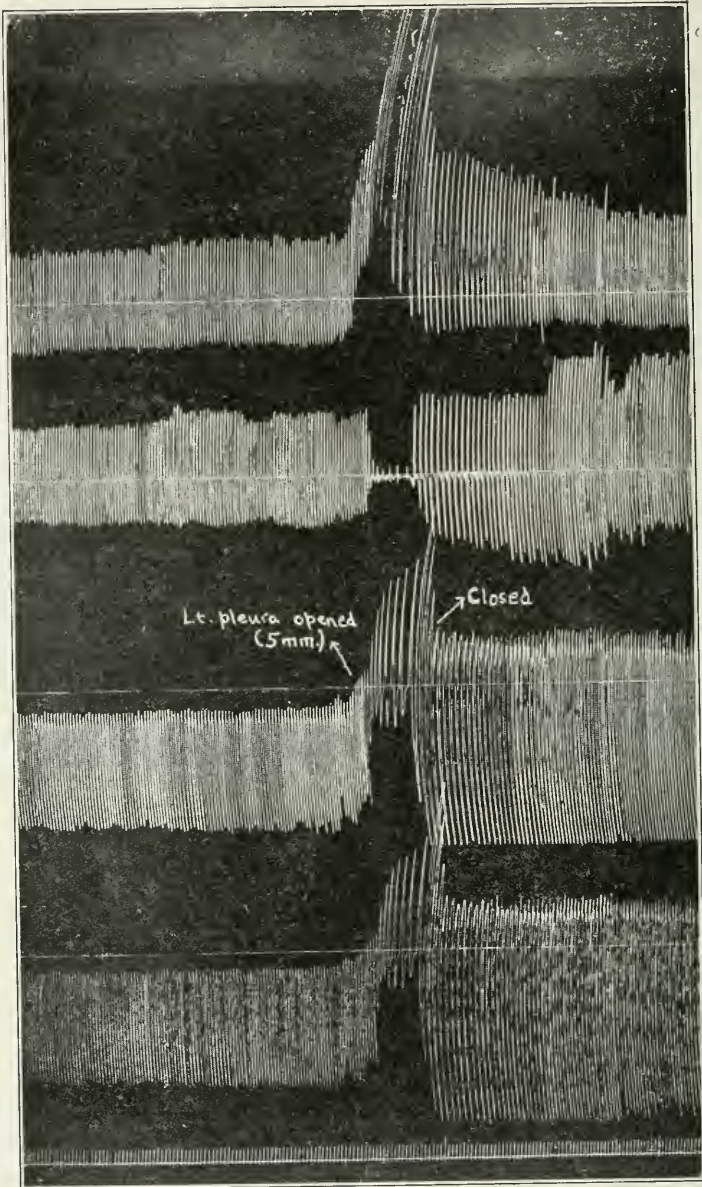
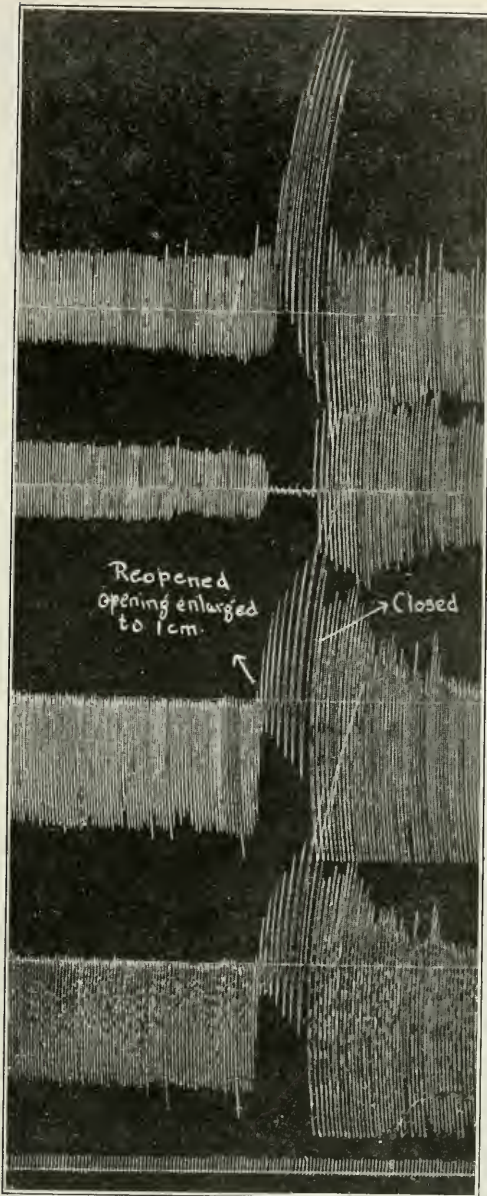


FIG. 4.—A tracing made on the living dog under ether anesthesia to show the nature of the reaction to an open pneumothorax with a moderate opening, as indicated in the changes in the respiratory movements, in the tracheal pressure and in the pressures in both pleural cavities. The upper tracings represents the respiratory movements, the next the tracheal pressure, the third the left pleural pressure and the fourth one the right pleural pressure. The lowest line indicates the time in seconds. The base lines were drawn at atmospheric pressure. The interval represents a duration of six minutes. Immediately after making the opening there is a simultaneous change of pressure in the pleural cavities from an entirely negative phase to one which



is mostly positive. The respirations are slowed but are increased in amplitude. Because the intrapleural pressure is largely positive, practically no air enters the trachea and the intratracheal pressure tends to be at equilibrium with atmospheric pressure. Immediately upon closure of the opening there is a simultaneous response in both pleural cavities, with restoration of negative pressure to a large extent, diminution of the amplitude of the respiratory movements and oscillations again of positive and negative intratracheal pressure, with inspiration and expiration. After an interval of six minutes during which time the air in the pleural cavities has probably been absorbed the intrapleural pressure has again become entirely negative.

be plainly seen to expand and contract with the inspiratory and expiratory efforts of the animal. Also, when a large opening is made, during the few minutes in which the animal remains alive the mediastinum can frequently be seen to flap from one side to the

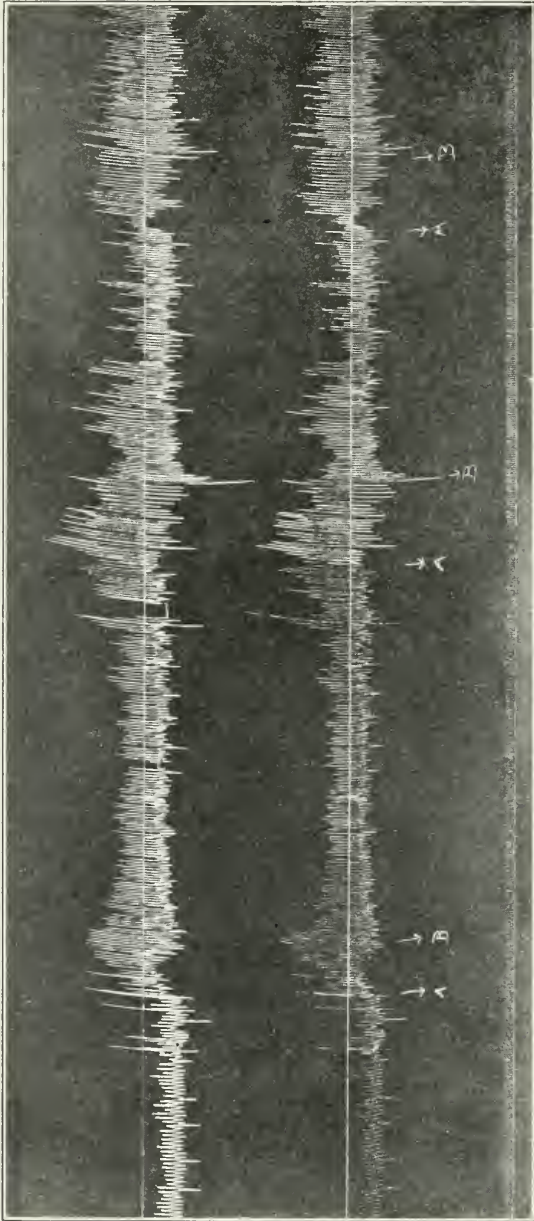


FIG. 5.—Tracing showing the simultaneous changes in intrapleural pressure in a dog when an opening of 5 mm. was made in the left pleural cavity with cocaine anesthesia. The base lines again represent atmospheric pressure. The upper tracing is the right pleural pressure and the lower that of the left pleural cavity. At *A* and *B* in each case the chest was opened and closed respectively.

other with inspiratory and expiratory movements in much the same manner as a flapping sail caught in the breeze first on one side and then on the other. It sometimes happens that, with a severe expiratory effort, the mediastinal pleuræ are ruptured so that a double pneumothorax occurs. The various points about the changed pressure relationship may be best understood by reference to the accompanying reproduction of tracings. (See Figs. 4 and 5.)

Influence of Posture on Effects of Open Pneumothorax. Elsbeg⁹ has raised the point that an animal with an open pneumothorax may be favorably or unfavorably influenced by posture. He quotes Depage as saying that the prone posture is the best in thoracic surgery. As a result of experiments on dogs he concludes that the prone position enables the animal to withstand an open pneumothorax much better than the supine or a lateral position. In three experiments of our own on dogs we tested out the influence of a prone and supine position respectively and we were unable to note any beneficial influence exerted by the prone position. In fact, with the animal lying prone the difficulties of compensating for the opening in the pleura were increased owing to the necessity for the animal with each inspiratory effort to raise his weight from the table in order to enlarge his thorax with his inspiratory muscles. It is interesting, furthermore, in this connection that Emerson¹⁰ after a most exhaustive review of the literature of pneumothorax states that "while, as a rule, the patient prefers to lie on the affected side there are two remarkable cases on record in which the knee-elbow position was chosen." Presumably the individual would choose whatever position would give him the most relief from his respiratory embarrassment, and the fact that there are only two cases on record in which preference was shown for a posture somewhat analogous to the prone would indicate that there is no decided relief gained usually from that posture. Probably the position which in a given case gives the greatest relief is somewhat dependent on the location of the opening and is brought about by the attempt on the part of the body to close the opening and thus to make a closed pneumothorax which, as will be shown later, causes the least respiratory embarrassment of all the types of pneumothorax if the amount of air enclosed is not too great. It seems possible that in the two exceptional cases quoted by Emerson the individuals had anterior openings.

Relation of Amount of Air Entering Thorax Opening to Amount of Air Entering Lungs. As has been mentioned earlier in this article the immediate influence of an open pneumothorax in producing respiratory difficulties depends upon the relation of the amount of air entering the pleural cavity to the amount of air entering the lungs.

⁹ Pneumothorax and Posture, Jour. Exper. Med., 1909, xi, 444.

¹⁰ Loc. cit., p. 390.

In the normal chest the action of the lungs, as a whole, proceeds practically as if no mediastinum were present, since the pressures in the two pleural cavities are always the same. If an opening is made into the chest cavity, part of the air which enters the chest during inspiration will pass in through the trachea and part will come through the chest opening. Only that part of the air which enters through the trachea is effective in carrying on respiration, and to prevent asphyxia the animal must increase either the rate or depth of respiration. If we assume that the rate of respiration remains constant and that all compensation is effected by increasing the depth of respiration, then the change of chest volume which occurs at each inspiration must be made greater by the amount of air which enters through the opening. That is, if the animal requires a volume of air (T), at each inspiration, and if a volume (B) enters through the opening, then the increase in chest volume at each inspiration must be $T + B$ after the opening is made.

If, however, the rate of inspiration is increased after the opening is made the volume of air required at each inspiration will be reduced. If the rate was R_1 before and R_2 after the opening was made then a volume of only

$$\frac{R_1}{R_2} T$$

will be required at each inspiration, and the required increase in volume of the chest to secure the same amount of air per minute will be—

$$\frac{R_1}{R_2} T + B$$

There is, however, a limit to the possible compensation. The change in the chest volume from maximum expiration to maximum inspiration is the same as the "vital capacity" V . The maximum possible compensation is reached when the increase in chest volume is V and when R_2 is the greatest possible rate comparable with this depth of respiration. Under these conditions it is evident that—

$$B = V - \frac{R_1}{R_2} T$$

represents the greatest volume of air that can enter through the thoracic opening if the animal is to survive even for a short time.

The ratio of the volume of air entering the chest through the thoracic opening to the volume entering the lung through the natural air passages would be equal to the ratios of their areas if it were not for two facts: (1) the natural air passages to the lungs have a considerable length which causes appreciable friction and a resistance to the entrance of air, and (2) the natural elasticity of the lungs

offers further resistance. On account of these two factors an opening in the chest wall of a somewhat smaller size than the narrowest part of the natural air passages will admit the same amount of air. If the area of this narrowest part, which is the glottis, is C , and if the resistance to the passage of air makes this opening equivalent to an opening of an area aC located in the thoracic wall (a being less than 1), then the entire ratio of the volume of air entering the chest through the thoracic opening to the volume entering the lung through the natural passages will be—

$$\frac{X}{aC}$$

X being the area of the thoracic opening. But from the equation above the maximum of this same ratio is—

$$\frac{\frac{B}{R_1}}{\frac{T}{R_2}} = \frac{V - \frac{R_1}{R_2} T}{\frac{R_1}{R_2} T}$$

and substituting we have—

$$\frac{X}{aC} = \frac{V - \frac{R_1}{R_2} T}{\frac{R_1}{R_2} T}, \quad \text{or} \quad X = \frac{V - \frac{R_1}{R_2} T}{\frac{R_1}{R_2} T} aC$$

In a normal human chest during rest the maximum area (X) of a thoracic opening compatible with life for even a short time can be obtained by substituting numerical values in this expression. The average vital capacity V and the tidal air T are given by Howell¹¹ as 3700 c.c., and 500 c.c., respectively. The normal rate of respiration R_1 during complete rest is about 15 per minute and the maximum rate R_2 for the greatest possible depth of respiration is about 60 per minute.

$$\frac{R_1}{R_2}$$

then equals 125 and

$$X = \frac{3700 - 125}{125} aC = 28.6 aC$$

The area of the human glottis may be taken as 2.25 sq. cm., and the value of a may be assumed to be about 0.8 for the maximum rate and depth of respiration. Therefore, $aC = 1.8$ sq. cm. and $X = 51.5$ sq. cm. In other words, an opening about 5 x 10 cm. (2 x 4.1 inches) is the

¹¹ Text-book of Physiology, Philadelphia, 1911, p. 646.

largest for which compensation can theoretically be established in the human even for short periods if the mediastinum has normal mobility. Practically, the opening must be somewhat smaller, since the extra work performed by the muscles of the chest to establish compensation increases the amount of air required. The presence of toxemia, infection or any other cause which increases the level of metabolism will decrease the safety limits of the maximum size of

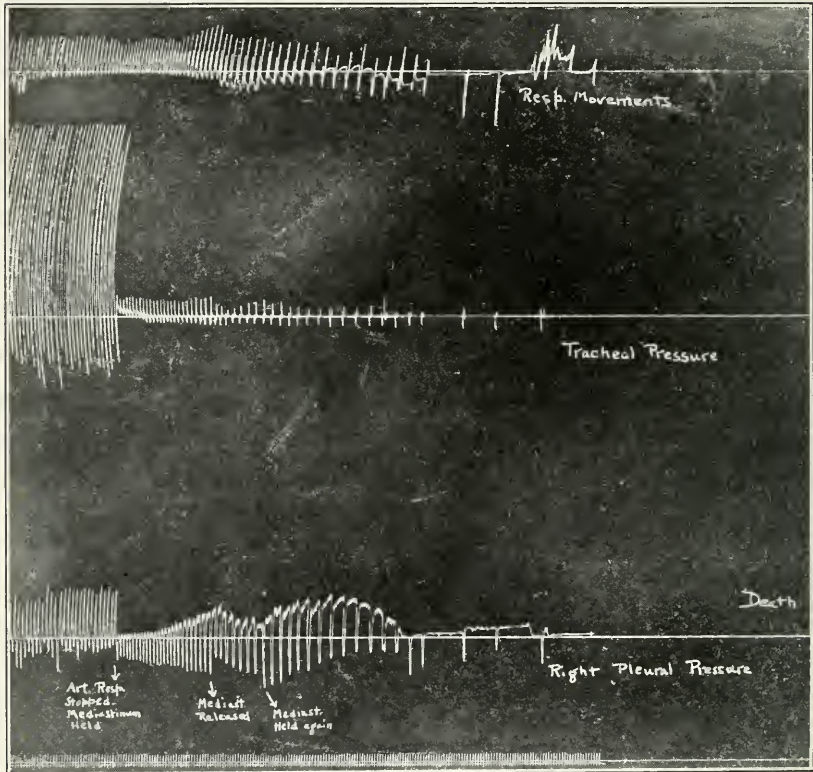


FIG. 6.—Showing slightly advantageous effect of holding of mediastinum in case of large opening into the left pleural cavity made by turning down a flap of pleura with six ribs while the dog was given artificial respiration by intratracheal insufflation.

the opening as will also any condition reducing the available breathing space of the lung. The use of general anesthesia will probably also act in the same way.

Effects of Immobilization of Mediastinum and Adhesions. Since the equalization of pressure in the thorax is dependent upon the mobility of the mediastinal structures, it would seem reasonable to suppose that any means of stabilizing the mediastinum would reduce the respiratory difficulties by confining the effects of the pneumo-

thorax to one pleural cavity. Old inflammation of the mediastinum with extensive induration will of itself result in a more rigid partition between the two pleural cavities. If, in addition to its being actually more rigid, the mediastinum is supported by strong adhesions the effect of an open pneumothorax on one side will be still less felt on the other. This is the condition which is often encountered in performing secondary operations of the type of Estlander, Schede, Delorme, etc., on old cases of empyema, and its presence probably accounts for the fact that in these operations the thorax can be opened widely with much less danger of respiratory embarrassment than is the case with the relatively normal mediastinum. These same factors also tend to make the deferred operation in acute empyema more safe than one performed too early. Experimentally, it can be shown that, furthermore, when the mediastinum is more or less fixed by pulling the lung well out of the pleural opening there is less pressure in the unopened pleural cavity than in the opened one. (See Fig. 6.) It is impossible, however, effectively to immobilize the normal mediastinum in that way because its extreme delicacy (especially in the anterior portion) allows it to be stretched and flapped about in spite of fixing it at one point by holding the root of the lung tight. It was hoped to demonstrate conclusively the influence which adhesions produced in various ways might have, but limitations of time have prevented it. The record of a single experiment, however, is presented. (See Fig. 7.) A few adhesions were produced between the lung and thoracic wall by the injection of 1 c.c. of turpentine. The record shows that during the intervals in which the left pleural cavity was open the right pleural pressure was distinctly less affected. On inspiration, for example, the pressure was twice as low in the right pleural cavity as in the left. This obviously enabled the dog to get more air into his lungs than he would have been able to do if the adhesions in the left pleural cavity had not to this extent prevented the aspiration of the mediastinum to the other side. Because of the elasticity of the lung tissue it is probable that extensive adhesions and those which involve the mediastinum itself are necessary in order to produce a more marked protective effect.

Closed Pneumothorax. In the description of the characteristic changes produced by making a free opening into the pleural cavity it was stated that the closure of the opening resulted in a sudden restoration of negative pleural pressure and a prompt relief from dyspnea. Obviously, after making the closure, air is still retained in the pleural cavity, so that the very striking difference in the phenomena observed must be due merely to the fact that an open pneumothorax has been converted into a closed one. Although air is absorbed from the pleural cavity, it disappears only slowly; and the sudden benefit noted by the closure of the opening cannot be attributed to the immediate disappearance of the air. Apparently

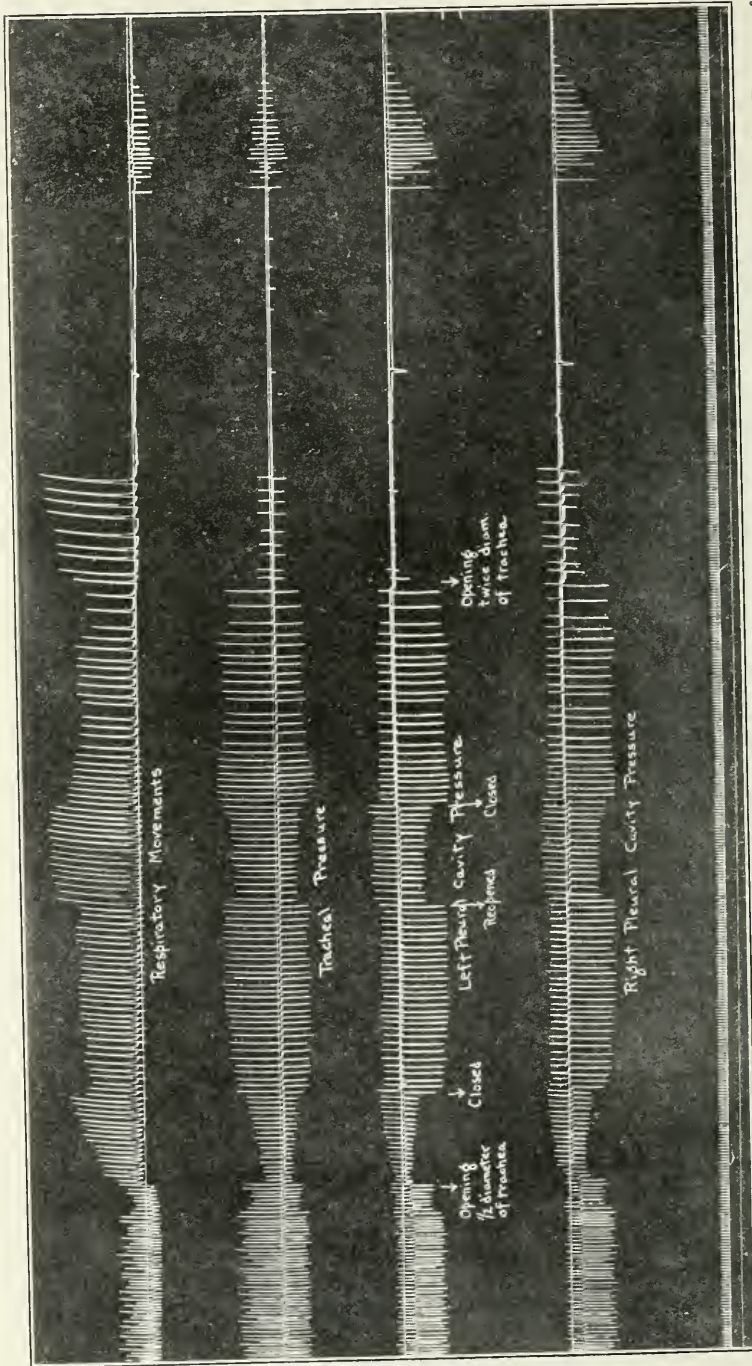


FIG. 7.—Adhesions between the left lung and thoracic wall. Opening made into left pleural cavity. Dog under ether anesthesia. Because of partial fixation of the mediastinum by the adhesions the right pleural cavity is less affected than the left. Respiration is maintained longer with the right lung than with the left, and there is more negative pressure on the right side than on the left when the left pleural cavity is opened.

the explanation of the relative harmlessness of a closed in comparison with an open pneumothorax lies rather in the fact that the ability to compensate for interference with the aëration of the lungs is limited. In a closed pneumothorax, no matter how much air is contained in a pleural cavity, no additional air can enter. It is necessary, therefore, only for the animal to increase his respiratory effort sufficiently to create enough negative pressure to allow him to take in the requisite amount of air to maintain aëration of his blood. Under conditions of rest this amount is equivalent only to the "tidal air," which in the human is about one-seventh of the total lung capacity. Accordingly, therefore, asphyxia should not occur until more than six-sevenths of the total lung capacity has been replaced by air in the pleural cavity, provided that the animal is at rest, that his ability to compensate by increasing his respiratory effort is good and that there is no extra abnormal demand for air such as might arise from toxemia. When an open pneumothorax is converted into a closed one, particularly if the closure is made at the end of expiration, the amount of air enclosed in the pleural cavity is very much less than six-sevenths of the total lung capacity, and naturally, therefore, there is comparatively little dyspnea. On the other hand in the case of an open pneumothorax there is an active competition for air going on between the trachea and the pleural opening. At each inspiration air not only enters the trachea but also enters the pleural cavity, and if the diameter of the pleural opening is the same as that of the trachea the same amount of air will enter the pleural cavity as enters the lungs and the animal will be compelled to increase his respiratory effort to get the "tidal air" in his lungs. If the opening is considerably larger than the trachea it will be still more difficult to get the required amount of air into the lungs, until when the pleural opening is of such size that more air than six-sevenths of the total lung capacity enters the pleural cavity with each inspiration the animal will no longer be able to obtain the requisite tidal air and he will die of asphyxia. This theoretical discussion is, of course, only an approximation and is not strictly accurate, since, as already shown in the paragraph dealing with the relationship of the diameter of the pleural opening to that of the air inlet to the lungs, it is necessary to consider the actual amount of air entering by each opening rather than merely the differences in diameter, a consideration which involves also the relative lengths of the pleural opening and the trachea with the resultant friction to the passage of the air. Observations, however, both clinical and experimental tend to confirm the truth of this explanation. For example, it is well known that an adult human can have as much as 2000 c.c. of fluid in his chest without producing alarming dyspnea so long as he remains at rest. Theoretically, he should be able to contain from 2500 to 3000 c.c. before developing a dangerous asphyxia if he remained quiet, and if it were not for the fact that his associated condition of toxemia and fever, uncompensated heart lesion, etc.,

demands a greater amount of oxygen than normal. Experimentally, we have injected into the pleural cavity of a dog of 8 kilos, through a small needle, as much as 1800 c.c. of air over an interval of twenty minutes without producing any marked asphyxia. Beyond that point, however, additional injections of only 50 c.c. at a time each had a very noticeable effect in increasing the dyspnea, and the animal died after about 2100 c.c. of air had been injected. The accompanying tracing illustrates the comparative harmlessness of a closed pneumothorax in which a moderate amount of air is present. Lest it should seem surprising that a dog of 8 kilos could withstand so large an amount of air as 1800 c.c. in his pleural cavity, it should be recalled that in proportion to the size of the rest of the body the dog has a much larger thorax than the human. (See Fig. 8.)

Effects of Open Pneumothorax other than Respiratory Disturbances. Besides its effects on respiration an open pneumothorax also induces other changes productive of harm to the body. These have been summarized by Sauerbruch¹² as heat loss, danger of infection and disturbances of the circulation. Sauerbruch himself has made some very important observations on the amount of heat loss. In unanesthetized rabbits in which he had established an open pneumothorax at a room temperature of from 20° to 22° C., the body temperature sometimes dropped as much as 3.5° C. within forty-five minutes. In dogs, also unanesthetized, within a half-hour he observed the body temperature fall 2° C. after making a pleural opening and rise again 1.6° C. within an hour after closing the opening. He also made the very striking observation that the heat loss in open pneumothorax is greater than in extensive laparotomy with eventration of the intestine for the same length of time. For example, a dog's temperature fell only 1° C. after having his intestine lying out of his abdomen for forty-five minutes, and a rabbit subjected to the same experiment showed a heat loss of only 1.3° C. after forty-five minutes.

The danger of infection is very great, since the ease with which organisms may be aspirated into the pleural cavity renders possible the infection of a relatively enormous amount of exposed surface. Naturally, also, a pleura already infected is exposed to secondary infection. That this readily occurs has been a frequent observation at Camp Lee in patients who had been operated on, and is a common experience to every surgeon. It explains, in many cases at least, the putrescent odor of the discharge so often present in old empyema cases. At Camp Lee we often found a great variety of bacteria after a pleural opening had been present for several days if means had not been taken to prevent the secondary infection, as by the use of Dakin's solution, etc. Ordinary aseptic dressing will usually not suffice to prevent the entrance of secondary invaders.

Marked disturbances in the general circulation have been noted by Sauerbruch as a result of the change of pressure relationships in the thorax, due to the pleural opening. He states that "in pneumo-

¹² Loc. cit.

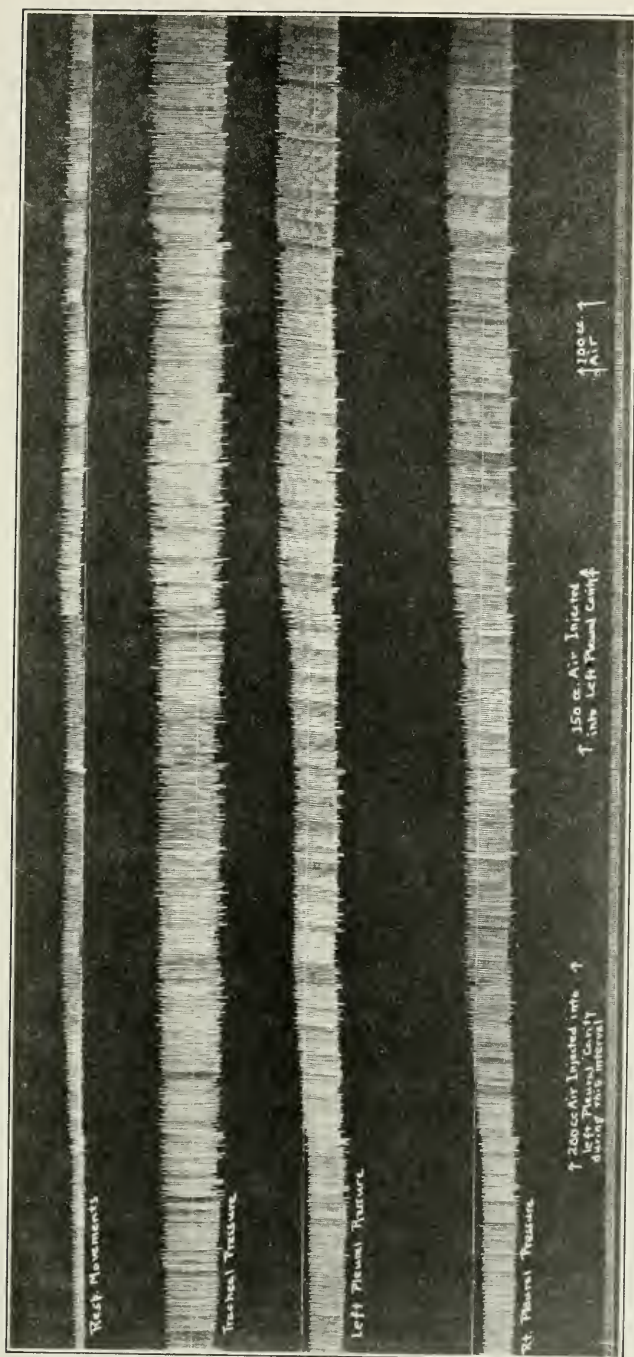


FIG. 8.—Closed pneumothorax in a 7-kilo dog under urethane anesthesia. It is to be noted that 450 c.c. of air can be injected into a pleural cavity without producing much distress, but again that the changes which result are strictly comparable in both pleural cavities.

thorax the aspiration of the heart fails; a stasis results in the venous system. Measurements of the venous pressure in the femoral vein give in fact an increase of the pressure." As a rule, there is not noteworthy change in the arterial pressure. When asphyxia occurs there is evident a rise in the carotid pressure, as might be expected. Sackur¹³ claims to have found a marked diminution in the amount of oxygen in the blood, in some instances to only one-half.

PART III.—EXPERIMENTAL EMPYEMA.

In order to test the applicability of these ideas of open pneumothorax to the surgical treatment of empyema a series of twenty dogs in which empyema had been produced was used. After several preliminary failures to produce an empyema by the intrapleural injection of from 10 to 15 c.c. of pure broth cultures of a virulent strain of hemolytic streptococci given to us by Major R. A. Kinsella,¹⁴ a successful result was finally accomplished by injecting into the pleural cavity of a 6-kilo dog 30 c.c. of a broth culture of the same strain which was highly virulent for mice. The dog died in about twelve hours after the injection, and at autopsy the left pleural cavity (the injected side) was found to contain about 200 c.c. of slightly blood-stained, serofibrinous fluid which contained myriads of streptococci and a few necrotic leukocytes. This exudate resembled in every respect the exudate obtained from the early human cases of streptococcus empyema at Camp Lee. Subsequently this exudate was used successfully in doses of from 1 to 5 c.c. for the production of empyema in the series of twenty dogs. In ten of the twenty dogs intercostal pleural drainage with cocain (0.5 per cent.) anesthesia was established from four to twenty-four hours after the operation. To the other ten dogs which served as controls nothing was done. The operations were all carried out under strictly aseptic precautions and sterile dressings were later applied. A stiff rubber drainage tube with a one-quarter inch (6 mm.) lumen was used for each dog and the tube was stitched to the skin in order to hold it in place. The point selected for the drainage in each case was the sixth interspace in the anterior axillary line, since this seemed to be the most dependent portion of the thorax with the dog in the natural position. Sixteen of the dogs each received 2 c.c. of the exudate, two each received 3 c.c. and two each received 1 c.c. All the injections were made into the left pleural cavity. The dogs were paired as carefully as possible according to weights, so that each dog operated upon had a control which was not only of approximately the same weight but which also had been injected with the same amount of pleural exudate. In general, out of each pair, the dog which seemed the stronger and the better operative risk was selected for the oper-

¹³ Weiteres z. Lehre von Pneumothorax, Arch. f. path. Anat. u. Physiol., 1897, cl, 151.

¹⁴ The particular strain used was the one which had been obtained at autopsy from the only fatal case of our series at Camp Lee. The patient had not only an empyema but also suppurative pericarditis and multiple small lung abscesses.

ation in order to give the operation every possible chance, since many of the dogs were poorly nourished and were victims of mange. In spite of all this, however, of the ten operated dogs all but one died (a mortality of 90 per cent.), and of the unoperated dogs only seven died (a mortality of 70 per cent.). Of the series of unoperated dogs also one fatality was in a dog which on the fourth day, while apparently well, was badly injured in a fight with another dog and received extensive lacerations in the neck, the back and the hind legs. Death occurred two days later and at autopsy the pleural cavity contained no exudate and appeared normal. It seems probable that it would not have died if it had not been for the wounds received in the fight.

It was a striking fact that of every pair of dogs which died the one which had been drained died from one to two days before its control with two exceptions, in which both the operated and the control dogs died at about the same time. It never happened that the unoperated dog of a pair died before the operated one. The only dog of the operated series which survived pulled its dressings off and pulled out the tube on the next day after the operation. When seen shortly afterward (within three hours after the dressings had been pulled off) the pleural opening had already closed so that the dog no longer had an open pneumothorax. This was the only dog which disturbed his dressings. As a rule, death occurred in the operated dogs from forty-eight to seventy-two hours after the operation, and in the control series from the fourth to the fifth day. Of one pair, each of which had been injected with 2 c.c. of the pleural exudate, both the control and the operated dog died after about twenty-four hours following the injection. The operated dog in this case had been drained four hours after receiving the injection. The operated dogs, as a rule, not only died more quickly than their controls but they all seemed much sicker than the unoperated dogs from the time that the pleural opening was made. They would lie quietly curled up, refusing food and resenting disturbance. The unoperated dogs were much more active. Immediately after operation each dog was placed in a cage by himself, was furnished with an abundance of water and food and the cage was kept clean. In almost every instance the dressings were changed daily, dry sterile dressings being substituted for the soiled ones, with rigid aseptic precautions, even to the extent of our wearing sterile gowns and sterile rubber gloves during the procedure. Each of the operated dogs had a profuse drainage of a thin serofibrinous discharge, sometimes slightly blood-stained, which microscopically showed innumerable streptococci and only a few leukocytes which were usually necrotic.

Each dog that died was examined at autopsy within a few hours after death. All of the operated dogs had been drained well, as shown by the absence of appreciable amounts of exudate in the pleural cavity. In practically every instance there was an extensive deposit of fibrin on the pleura, and there were many recent adhesions.

In general there were more adhesions in the dogs that had been drained than in the controls. Two dogs showed in addition to a left pleuritis involvement of the pericardium and the other pleura also. It was interesting that the pericardial fluid contained a noticeably smaller amount of organisms than the left pleural cavity and that the right pleural exudate contained even fewer. In other words, it appeared as if the infection had passed right through the pericardium and mediastinum from the inoculated left side. Of these two dogs, one had been drained and the other had not been. Three of the dogs that had been operated upon showed at autopsy pockets of pus behind the upper part of the sternum which resembled very much those which had been described frequently in the human cases. This condition has never been observed in any of the dogs which were not drained.

The fact that in this series there was a slightly higher mortality in the dogs that had had early drainage than in a control series of the same number which received no treatment of any kind seems to indicate very strongly that under the conditions of the experiment, early drainage at least is of no benefit to the animal, and if anything it is rather a source of harm. Presumably the harm is produced by the open pneumothorax, with the train of resulting effects which have been discussed earlier in this article. Any comparison, furthermore, with the condition of streptococcus empyema in man must carry with it the important consideration that theoretically this experimental empyema in dogs does not begin to contra-indicate the early establishment of an open pneumothorax to the same extent as the human condition for the reason that the dogs do not have the associated pneumonia which seems to have been universally present in the human cases and which necessarily lowers the threshold of safety for the establishment of an open pneumothorax. It was hoped to test out early aspiration with later operation on another series, but time was not available for the experiment.

PART IV.—EXPERIMENTAL PNEUMONIA.

Attempts were made to produce in dogs the typical pneumonia and empyema of the human cases. It was felt that success in the experimental production of the condition would not only allow a better opportunity to determine by experiment the best treatment of the condition, but that also an opportunity would be presented of perhaps studying the pathology in all of its various stages with particular reference to the factors underlying the occurrence of empyema. Here, again, unfortunately, it has been impossible to carry this part of the work to a conclusion because of lack of time. We have, however, been able in three out of six dogs to reproduce a condition experimentally which seems to be in every way identical with the pathological picture of the human pneumonia and empyema which has been so well described by Dr. W. G. MacCallum. The

method used was tracheal insufflation of pleural exudate from other dogs into a dog deeply anesthetized with ether. The amount of pleural exudate used has varied from 2.5 to 5 cm. One of the dogs in which a successful result was obtained also was moderately ill with distemper at the time the insufflation was made. A brief summary of one of the experiments with a gross description of the viscera of the dog as noted at autopsy is as follows:

An 8.5-kilo dog on August 28 was given 2 c.c. of pleural exudate by method just described above. On August 31 the dog died. There was a very extensive pneumonia of both lower lobes with scattered areas of consolidation in the other lobes. Bilateral empyema (200 c.c. thin, slightly purulent fluid in left pleural cavity and 100 c.c. in right pleural cavity) was found, as well as suppurative pericarditis (about 50 c.c. of exudate in the pericardial sac similar to the pleural exudate) with extensive deposition of fibrin on the pericardium. Extensive fibrinous adhesions were present in both pleural cavities with massive fibrinous deposits on the posterior surfaces of both lower lobes. Each lower lobe also showed posteriorly a necrotic patch about 1 cm. in diameter which was found to allow air to escape when attempts were made to inflate the lungs, according to MacCallum's method. It seemed in fact that on the right side there was a pneumothorax in addition to the empyema, as air apparently escaped from that side when it was opened. We were not sure, however, of this point. The tracheobronchial glands were much enlarged and there was a moderate tracheitis. The other organs showed no important changes. The lungs were not cut but the thoracic viscera were placed *in toto* in Kaiserling solution. A description of the appearance of the cut surface of the lungs will be included in the report on the microscopic examination by Dr. MacCallum.¹⁵

¹⁵ Incision into the several lobes on each side reveals areas of reddish-gray consolidation most extensive in the lower lobes. There is on each side in the central portion of the area in the lower lobe a ragged cavity filled with fluid and necrotic material and extending to the pleura, which is torn so that the abscess cavity appears in both cases to have communicated with the pleura. Other smaller areas appear opaque and necrotic, but are not liquefied. Microscopically it is found that the pleura is thickened and covered with a fibrinous exudate. No broad lymphatics are traceable into the substance of the lung. The bronchi are filled with leukocytes, among which are very numerous streptococci. Their walls are not markedly altered, although the epithelium is frequently desquamated. No conspicuous or thrombosed lymphatics are seen in their walls nor in the walls of the bloodvessels. The alveoli are filled with an exudate of polymorphonuclear leukocytes, with some red corpuscles and great numbers of streptococci. Their walls are not infiltrated or thickened. Great areas in the midst of such consolidated tissue have become necrotic *en masse* and are surrounded by a zone of closely packed leukocytes. These areas, rich in streptococci, are sometimes intact, but the larger ones show a complete disintegration of the structure of the necrotic lung and of the enclosed exudate, and the softened, partly liquefied debris is seen to have retracted from the living tissue, which remains as a densely infiltrated wall. The consolidation has little in common with the interstitial bronchopneumonia observed in the recent epidemic, but is almost precisely like the condition also observed then which was referred to as lobular pneumonia. In that condition large numbers of streptococci invaded the lungs, causing a widespread intra-alveolar exudate, with hemorrhage and subsequent extensive necrosis of the infected tissue. The sections from the second dog repeat this picture so precisely that they need not be described.—W. G. M.

PART V.—GENERAL DISCUSSION.

Application of Experimental Results to Problem of Treatment of Empyema. In the light of all these observations it would seem definitely established that an operation for empyema performed too early in the course of the disease is accompanied by such very grave danger that in our opinion the risk of harm by the operation outweighs any advantages which it may have. These observations apply particularly to the type of empyema due to the hemolytic streptococcus prevalent in the epidemic last winter, but apparently they would apply equally well to any type of empyema. The principal determining factors to be considered in deciding whether the time is too early for operative interference are the relative immobility of the mediastinum, the presence of active severe pneumonia and the amount of asphyxia present. Practically it may be stated that, in general, the safest time to operate is when the exudate has become frank pus instead of being merely serofibrinous, for the following reasons: (1) There is less danger of creating an open pneumothorax because, in our experience, there is likely to be a circumscribed abscess shut off by adhesions from any communication with the free pleural cavity so that during the operation the pleural cavity, properly speaking, is not entered. (2) Even if an open pneumothorax is created the patient is in much better condition to withstand its harmful effects, because (a) the subsidence of the active pneumonia has the effect of making the area of the air-inlet to the lungs larger than when many of the bronchioles and much of the lung parenchyma are blocked by the pneumonic process, so that the pleural opening is incapable of producing the same amount of harm, (b) the presence of adhesions and the inflammatory thickening and induration of the mediastinum tend to make it less mobile, (c) the patient's need of oxygen is less because of a more nearly normal metabolism, (d) the respiratory compensation is more efficient since, owing to a diminished toxemia, the respiratory muscles will not become so easily fatigued. (3) The patient is in better condition to withstand whatever shock there is connected with even so slight an operation as pleural drainage. (4) There is probably less risk of creating a septicemia from absorption of organisms from the fresh operation wound, an occurrence which seemed to have happened a few times at Camp Lee by the finding of positive blood cultures a few hours after operation in cases which previously had shown negative blood cultures, the operation having been done very early in the disease.¹⁶

On the other hand the only advantage to be gained from an early operation is drainage which theoretically accomplishes the removal of both toxic material and living organisms and in addition relieves

¹⁶ For our usual procedure in deciding when to operate upon cases of streptococcus empyema at Camp Lee, see "Preliminary Report of Empyema Commission," Review of War Medicine and Surgery, Office of the Surgeon-General, Washington, 1918, i, No. 6, also Jour. Am. Med. Assn., lxxi, 1918, 366 and 443.

mechanical embarrassment to respiration caused by the presence of a large amount of fluid. Practically, however, the mechanical embarrassment to respiration is almost sure to be aggravated instead of improved because of the creation of an open pneumothorax; and, moreover, the fluid can be withdrawn by aspiration as often as it accumulates in any considerable amount, a procedure which, of course, also removes some of the toxic material and living organisms. The apparently theoretically ideal method of continuous drainage under negative pressure involves the necessity of a special attendant to prevent a delirious patient from interfering with the apparatus and thus running the risk of creating an open pneumothorax. It should not be forgotten also that in many of these streptococcus cases operation will be unnecessary. Of our cases at Camp Lee, 13 per cent. recovered merely with aspiration.

If, in spite of consideration of all the relative dangers of an early operation, it should be decided nevertheless to establish drainage in a certain case, it seems apparent that only a small opening should be made during the stage of active pneumonia. Resection of ribs and the creation of large openings in the pleura should be reserved if necessary, until later, after adhesions and induration have changed the mediastinum into a relatively immobile partition.

In considering the mathematical expression given in a previous section it will be seen that any condition which increases the values of

$$\frac{R_1}{R_2} T$$

or which decreases the value of V or of aC will decrease the size of the maximum opening compatible with life. Thus any obstruction of the natural air passages, any interference with maximum contraction or expansion of the chest or any condition which increases the demand for air will tend to decrease the limit of safety in the size of the opening. In the early stages of a streptococcus pneumonia several such factors are present. There is great obstruction of the air passages, and the vital capacity is reduced by the consolidation of the lung and by the exhausted condition of the muscles of respiration. The amount of air required is greatly increased since the general metabolism is nearly doubled. All these factors tend to reduce the size of the thoracic opening for which compensation can be made by the patient. In fact, some cases have already so much interference with respiration that they are partially asphyxiated and a thoracic opening of any appreciable size must inevitably cause death.

On the other hand a patient who has recovered from the pneumonia and presents only an empyema is in a much more favorable condition to stand an open pneumothorax. The air requirement has fallen considerably, the obstruction of the air passages and the consolidation have disappeared, and the muscles of respiration have recovered from their exhaustion. The mediastinum has become thickened and stiffened by exudate and immobilized by adhesions so that it no longer has normal mobility, thus reducing greatly the effect of a

pneumothorax on the lung of the unoperated side. The presence of this condition may make the patient even a better operative risk than a normal man.

There is no Discrepancy between our Experimental Results and the Clinical Findings in War Wounds of the Thorax. During the past year the idea has become prevalent in this country that operations upon the thorax which permit of the free entrance and exit of air into the pleural cavity during the operation can be performed with about the same impunity as abdominal operations. In fact, the belief has arisen that surgeons at the front have found that alterations of the intrathoracic pressure by the admission of air through extensive incisions or large gaping wounds are in themselves not dangerous, and a feeling of optimism exists that now bold surgical intervention on the thorax may be carried out. It has been said consequently that the danger from creating an open pneumothorax in early operations for empyema with permanent drainage is negligible. These conceptions apparently have been largely based upon the address made a year ago at the Clinical Congress of Surgeons by Sir Berkeley Moynihan, a Colonel in the Royal Army Medical Corps. In the printed address Colonel Moynihan¹⁷ bases his remarks chiefly upon articles by Duval, Depage, Gregoire, Elliott, etc. He says practically nothing about how extensive his own experience with wounds of the lungs and pleura has been, but he makes some remarkable statements which give the impression that the operator may attack the lungs boldly without heed to the danger of an open pneumothorax. For example, in discussing the open operation for extraction of foreign bodies he states that "no shock follows this operation," also, that during the operative incision of the pleura the free admission of air, "as a rule, causes no disturbance and does not alter the rate of the respirations or of the pulse."

On the other hand, reference to the work of Duval¹⁸ and of others who have had extensive personal experience with this type of cases gives one a very different impression from that obtained from Moynihan's address, although at their hands also results were obtained which seem startling when compared with our ideas of the limitations of thoracic surgery before the present war. For instance, Duval's article, which is based on 3453 cases, shows that of all types of wounds of the chest the mortality is nearly twice as great in the gaping as in the closed wounds (27 and 15 per cent. respectively). The larger mortality of the gaping wounds is ascribed by Duval chiefly to the element of infection, but it seems highly probable that many of these may have died of the open pneumothorax, especially since, according to Duval, 50 per cent. of all lung wounds die within the first day, before the results of infection could have manifested themselves. Piéry states that the two gravest prognostic

¹⁷ Gunshot Wounds of Lungs and Pleura, Surg., Gynec. and Obst., 1917, xxv, 605.

¹⁸ The original was inaccessible to us, but extensive abstracts of the work of Duval and others may be found in the Review of War Surgery and Medicine, Office of the Surgeon-General, Washington, 1918, 1, No. 4, 1-27.

elements are the large, open chest wound and generalized infection. "In discussing operative indications, Piéry¹⁹ sounds a moderate note of conservatism when he points out that he considers it unfortunate that the early optimistic reports regarding the safety of lung surgery must in a measure be modified—in other words, one must bear in mind that surgery of the lung, in spite of the remarkable recent advance, is still surgery of a very grave sort." Both Duval and Piéry consider that the gaping wound must be closed in order to overcome the resultant mechanical embarrassment of respiration and the resultant pleural infection. As a matter of fact, according to them, closure is to be considered as an emergency operation.

As regards the operative attack on the lung itself it is to be noted that most surgeons with wide experience in war wounds of the lungs adopt measures which of necessity tend to limit the actual area of the opening into the pleural cavity and also to immobilize the mediastinum somewhat. In other words, they follow either consciously or unconsciously methods which our experiments show to be effective in reducing the danger arising from an open pneumothorax. For example, as a rule, the lung is drawn out through the thoracic incision a procedure which not only diminishes, if it does not actually plug, the opening into the pleura, but also tends to immobilize the mediastinum. Moreover, generally, the thoracic opening is plugged by a thick gauze compress after the delivery of the lung in order to obviate the to-and-fro movements of air during the operation. "It²⁰ is necessary to operate as gently and quickly as possible and to get the opening in the chest wall closed at the earliest possible moment. In case there should be any evidence of mechanical interference with breathing it is advisable rapidly to deliver the lung, plugging the chest wall with gauze. This procedure is usually followed by cessation of all respiratory embarrassment." Duval says that the closure of the chest wall must be done very carefully in order to avoid the leakage of air; the resected rib ends should be covered with muscle in order to get an air-tight wound. "Although the operation is described as sometimes remarkably simple it is, nevertheless, exceptional for these patients to run other than a rather stormy postoperative course." Roberts and Craig,²¹ in a report based on 199 cases state that they operated upon "open" cases so soon as the condition of the patient permitted and that before doing that the great majority of cases in this class never reached the base. Anderson²² in an experience in a British casualty clearing station found that the closure of an aperture in the wall of the thorax more than compensates for any risk which is accepted, and he emphasizes that the important matter is to get the chest completely closed. Gask and Wilkinson²³ in a report based on 500 cases of this type, also at a British casualty clearing station, adopted

¹⁹ Quoted from Review of War Surgery and Medicine, loc. cit., p. 10.

²⁰ Quoted from the combined abstract in the Review of War Surgery and Medicine, loc. cit., p. 14.

²¹ Ibid., p. 18.

²² Ibid., p. 20.

²³ Ibid., p. 22.

the routine of always closing large openings into the pleura through which air was sucked by temporary skin suture without an anesthetic. This was found to give the patient immediate relief.

It is evident, therefore, that from the experience of many surgeons in a very large series of war wounds of the chest the dangers arising from an open pneumothorax cannot be disregarded. On the contrary it is not surprising that otherwise healthy men can stand during the period of an operation a relatively large opening in the thorax, for in a previous section of this article it is shown that on the basis of calculations based on our experiments a healthy adult, without pneumonia and with good respiratory muscles, should be able to stand for a short time without death an opening of about 51.5 sq. cm. (5 x 10 cm., or 2 x 4.1 inches). It should be emphasized that, on the basis of our calculations, this is the largest possible opening compatible with life in the average healthy adult with a normal mediastinum, and that life can be maintained with so large an opening for only a short time. It is larger, however, than the usual area of an opening into the chest when an operation is made on the lung, especially when the opening is partly closed by the presence in the incision of a hand, the lung, a gauze pad or a number of instruments. *There is, therefore, no discrepancy between the deductions drawn from our experiments and the clinical observations on war wounds of the chest.*

Mechanism of Reaction to Change of Intrathoracic Pressure not Clear. The almost instantaneous response in the character of the respiratory movements which follows the creation of an open pneumothorax cannot be satisfactorily explained at the present time. It is very unlikely that asphyxia can account for it because the reaction occurs before any appreciable effect of asphyxia on the respiratory center can manifest itself. Also, that it is not due to the stimulation of nerve endings by the admission of cold air into the pleural cavity is shown by the fact that on several days when experiments were performed the temperature of the room was between 95° and 100° F. No noticeable difference was detected at this temperature and at lower temperatures.

Summary and Conclusions. From the standpoint of pressure relationships the normal thorax may be regarded as one cavity instead of two. Any change of pressure in one pleural cavity is accompanied by practically an equal change in the other so that an equilibrium of pressure exists at all times throughout the whole thorax. In our experiments the changes of intrapleural pressure have been accomplished only with air, but probably the same conclusions would hold for those effected by fluid.

The prevalent conceptions of pneumothorax are erroneous in that they are based on the assumption that when an opening is made into the chest one lung is collapsed and the other maintains respiration. This assumption implies that the mediastinum constitutes a rigid partition between the two pleural cavities. On the

contrary the mediastinum is so mobile that any increase of pressure in one pleural cavity pushes it over into the opposite one so that both lungs are compressed practically equally. No such condition is possible, therefore, of collapse of one lung and maintenance of respiration with the other in a chest with a normal mediastinum.

If, on the other hand, the mediastinum has been made rigid by induration as a result of long-standing inflammation, or if it has become fixed by adhesions, then a pleural opening on one side will not produce the same pressure changes in both pleural cavities.

The maximum opening into a pleural cavity compatible with life depends upon a definite relationship which exists between the amount of air entering the lungs and the amount which enters the pleural opening. The maximum opening compatible with life may be approximately determined for the normal chest by the mathematical expression given in the text. By this mathematical expression it is found that a normal human adult should be capable of withstanding for a short time an opening of about 51.5 sq. cm. (5 x 10 cm., or 2 x 4.1 inches). There is no discrepancy, therefore, between our experimental results and the finding at the front that men are capable of maintaining respiration with gaping thoracic wounds, which seem surprisingly large.

A double open pneumothorax in a normal chest is more dangerous to life than a unilateral open pneumothorax merely because usually the combined areas of the two openings (and therefore the amount of air admitted into the pleural cavities) is greater than a single opening on one side is likely to be. Theoretically and experimentally effects of practically the same severity result in the case of one or more openings into one pleural cavity as follow the creation of a double pneumothorax, provided that in each case the combined areas of the various openings are equal.

The bearings of these results and deductions upon both the treatment of acute empyema and upon thoracic surgery in general is obvious. Whenever the amount of air taken into the lungs is limited by the presence of an active pneumonia, with plugging of both air channels and alveoli, whenever there is an excessive demand for air, or whenever there is sufficient weakening of the respiratory muscles to impair compensation, the size of a pleural opening compatible with life becomes smaller; and if any or all of the above factors are present in sufficient intensity, even a very small opening into the pleural cavity will produce death from asphyxia. Since all of these factors are likely to be present to a high degree during the early stage of an empyema of the streptococcus type, early operation with the establishment of an open pneumothorax carries with it an unwarrantable danger. Aspiration is indicated instead until after the above dangerous factors have disappeared.

Special emphasis has been placed in this article on the changes of intrathoracic pressure induced by an open pneumothorax, but other results such as heat loss, danger of infection and disturbance of the systemic circulation are of great importance.

IRRITABLE HEART OR EFFORT SYNDROME.

BY CAPTAIN THAYER A. SMITH, M. C.,

CARDIOVASCULAR SPECIALIST,

AND

MAJOR DAVID BOVAIRD, M. C.,

CHIEF OF MEDICAL SERVICE, CAMP DIX, NEW JERSEY.

THE medical work incidental to the selection of men for our new armies has brought new problems and novel experiences for all engaged in it, even for those who by reason of years of service in civil or military hospitals might justly consider themselves familiar with the various fields of clinical medicine. Especially is this true with relation to the physical signs and phenomena of heart affections. Not indeed that anything essentially new has been discovered, but rather that the methods employed, applied as they have been to many thousands of men called from civil life to the Colors, have brought new appreciation of the extent to which certain physical defects or disturbances prevail among our people and have compelled us to study these conditions from an entirely new view-point, that of the acceptability of the subject of such disabilities for military service. The problem has concerned prognosis rather than diagnosis, and its solution has been hedged about with anxiety, both for the welfare of the individual concerned and for the soundness and vigor of our armies.

To rightly value the facts set forth in this report certain considerations must be borne in mind. In the first place the men summoned for military service must have been subjected to most careful and repeated physical examinations. It is doubtless true that no army in the world has been put through so many tests to assure the physical soundness of its personnel. The men of the National Guard were not only examined by their regimental surgeons before being mustered into the Federal service, but were also gone over, man by man, by experts in the diagnosis of diseases of the heart and lungs. The drafted men were examined at the place of their enrolment and again at the camp to which they were assigned. In the case of any suspicion of disability they underwent a third examination at the hands of specialists in the particular field concerned. Finally, in all the camps during the past six or seven months, boards of specialists in tuberculosis have been engaged in going over the forces, man by man, for disease of the heart or lungs. In consequence of these methods it may safely be assumed that few indeed of the recruits presenting any abnormality of heart sound or action have escaped observation. As a corollary the numbers of those found or believed to be suffering from disease or disturbance of the heart has been impressively large.

The problem of the disposition of these cases has been one of the most difficult with which the army medical staff has had to deal. Their numbers made it a matter of importance that they should not be released from service without sound grounds for that action, and yet they could not be held without anxiety as to what the future might develop with regard to their suitability for service, especially in the event of their being sent overseas. The gravity of these questions has forced upon those concerned the most careful restudy and restatement of the criteria of both organic and functional heart affections and the most painstaking application of the conclusions to the individual case.

In this difficult undertaking we have had, as in all our preparations for this great war, the invaluable aid of the experience of the nations now our allies, and especially that of the British and Canadian armies. The results of that experience are embodied in the "Reports upon Soldiers Returned as Cases of 'Disordered Action of the Heart,' " or "Valvular Heart Disease," published under the auspices of the British Medical Research Committee. This report summarizes the work of a large group of investigators and covers, in a comprehensive manner, the whole subject of cardiac affections in relation to military service. From it has been taken the caption under which Dr. Thomas Lewis prefers to designate the particularly interesting group of cases previously described as "Cardiac Palpitation" or "Irritable Heart," which has been made the subject of our study.

The affection is by no means a new one. During our Civil War it was observed and studied thoroughly by Da Costa. The reader of his scholarly article¹ will at once see that he is dealing, in general, with the same class of cases that we are meeting today. Moreover, he finds some reference to the affection in the British reports on the Crimean War and very justly surmises that it has always prevailed among soldiers, but has heretofore escaped detection by reason of the difficulties of distinguishing it from organic lesions of the heart.

Da Costa gives the "general clinical history" of a considerable number of his cases as follows:

"A man who has been for some months or longer in active service would be seized with diarrhea, annoying, yet not severe enough to keep him out of the field; or if attacked with diarrhea and fever he rejoined, after a short stay in the hospital, his command and again underwent the exertions of a soldier's life. He soon noticed that he could not bear them as formerly; he got out of breath, could not keep up with his comrades; was annoyed with dizziness and palpitation and with pain in the chest; his accoutrements oppressed him, and all this though he appeared well and healthy. Seeking advice from the surgeon of his regiment it was decided that he was unfit for

¹ Irritable Heart, AM. JOUR. MED. SC., January, 1871.

duty, and he was sent to a hospital where his persistently quick-acting heart confirmed his story, though he looked like a man in sound condition. Any digestive disturbances which might have existed gradually passed away, but the irritability of the heart remained, and only very slowly did the excited organ return to its natural condition; or it failed to do so, notwithstanding the use of remedies which control the circulation; thus the case might go on for a long time and the patient, after having been the round of hospitals, would be discharged, or, as unfit for active duty, placed in the Invalid Corps."

With the exception that diarrhea or any other digestive disturbance is a rare antecedent, the above clinical picture is fairly representative of the condition as we have observed it.

In like manner his description of the symptoms and physical signs of the affection, both remarkably painstaking and accurate, for the most part, fit the conditions as we find them. His data being necessarily limited to the results of physical examination and clinical observation, without the instruments of precision whose use of recent years has added so much to our knowledge of the affections of the heart, he had included in his groups certain cases which we would now place in other categories. There are, for example, a few cases of auricular fibrillation and some also of probable myocarditis and cardiac hypertrophy. The great majority of his cases, however, appear to be identical with those presented in this report.

It is true, also, that Da Costa, though he notes in some instances that the disability had existed prior to the enlistment, and also states that he could parallel his observations among the soldiers with cases from private practice, nevertheless regards the affection as peculiarly related to the military life. One would infer that whatever examination was made before the acceptance of a recruit at that time it was not adequate to bring out the defect. In consequence this was discovered only when some acute illness or unusual exertion aggravated the disturbance and rendered the soldier unfit for duty. The careful medical supervision given our new armies brings out the fact that many of the recruits have this disturbance at the time of their reception and, as is pointed out in the present report, have had it for some years before their entry into the service. It therefore belongs to the soldier's life only in the sense that the physical exertions required of him, or the hardships or illnesses incident to his occupation, bring it to the fore.

The query naturally arises why, if this be true, the subject has received so little attention in clinical medicine since the publication of Da Costa's paper, and only the calling of great numbers of men to military service has again brought it into prominence and made it the subject of thorough study. The explanation would appear to be that, under the ordinary conditions of civil life, men suffering from this disability early become conscious that they are unequal

to heavy or exhausting physical labor and betake themselves to some form of occupation for which they are competent. In this way they make the best of the matter and get along tolerably well until such time as the disturbance in its natural course passes off. They only comparatively rarely present themselves for study or treatment and their affection under ordinary conditions receives scant attention. One may search the works of Babcock, Broadbent, Brockbank, Brunton, Hart, Mackenzie, Morison and even Lewis (until the report already referred to) without finding mention of the work of Da Costa or appreciation of the importance of the subject. In Hoover's article on "Irritable and Weakened Heart"² there is a paragraph devoted to Da Costa's observations.

In our present war conditions the subject becomes one of importance. In every camp one will find numbers of men suffering from this disorder under observation and study to determine the propriety of holding them for military service. No small part of the rejections for physical disability among the new recruits are made for this reason. For example, one-fifth of the rejections for cardiac complaints in Camp Dix up to February 1, 1918, had been made on this ground. In the exigencies of the present situation it was thought best to release many men from the service, although it was regarded as possible that by proper handling some of them might in time have been rendered fit. Efforts along these lines are now being made. It is therefore highly important to understand, as thoroughly as possible, the problem these patients present. The study embodied in this report was made to the end of increasing our knowledge of the condition and enabling us more effectively to deal with it.

While it has not been practicable to install the electrocardiograph in the base hospitals, the sphygmomanometer, the polygraph and the roentgen rays have been available and have been freely used. With these aids to accurate diagnosis and the knowledge which recent intensive study of diseases of the heart has made common property we approach the differentiation of functional and organic affections of the heart with confidence, and in dealing with these patients we feel reasonably certain that careful study will enable us to exclude the presence of organic lesions and, in our handling of them, avoid doing them harm.

The observations herein reported were made upon cases sent to the cardiac consultant for office examination, not for observation in the hospital wards. This series includes most of the severer cases met with, but many of the milder cases have not been recorded here. In some instances only a single examination has been made; many of the cases have been seen twice and a number three or four times, the findings on subsequent examinations being practically identical

² Osler: *Modern Medicine*.

with those at the first visit. No case was diagnosed as of this type which presented any definite evidence of organic heart disease, and pulmonary tuberculosis, general neurasthenia and the tachycardia immediately following a febrile affection were carefully excluded. It was found very difficult to exclude hyperthyroidism, but when this diagnosis seemed reasonably certain it was made. Many of these cases were referred by the regimental surgeons for advice as to diagnosis and disposition; some were referred by the Board of Examiners for Tuberculosis, some by the Disability Board and a few by the ward surgeons of the Base Hospital. They were variously diagnosed as effort syndrome, chronic myocarditis, cardiac dilatation, simple tachycardia and valvular disease with poor compensation.

Occupation. A. Indoor occupations predominate.

Indoor	33 cases.
Outdoor	17 "

B. Little difference was noted as to whether sedentary, light or heavy work was engaged in.

Sedentary	14 cases.
Light	23 "
Heavy	13 "

Da Costa attributed no influence to the preceding occupation, remarking only that "painters, butchers, blacksmiths, carpenters, the city-bred man who had left his desk in the counting-house and the farmer fresh from tilling the fields were all fully represented in the long list of sufferers."

On the other hand the British Commission reports that of 543 instances in which this point was investigated, 57 per cent. were from light or sedentary occupations, 20 per cent. from moderately heavy employments and 23 per cent. from heavy work. They discuss these data in the following terms:

"The incidence is extraordinarily heavy among men engaged in indoor and sedentary work before the outbreak of the war. This fact may be accounted for in several ways: A large percentage of the patients were affected by the condition in civil life and years before joining the army; of these many had been forced to adopt sedentary occupations and had given up heavier work earlier in life because of their unfitness for it. The condition is commonest among civilians, often precluding heavy work; usually it does not preclude sedentary work or light work; affected civilians therefore tend to drift into these employments, and once they are so employed they are able to carry on with some slight degree of discomfort or they may be entirely free of symptoms. A history of each kind is common. Thus the men frequently relate that they were well once sedentary work was adopted, but they were unable to engage in outdoor games or exercises. But it is equally clear that a more considerable number

entered sedentary occupations for other reasons. Of these some became aware that they were unfit for violent exercise at a later date; others had never so tested themselves and the symptoms of these often date from the earliest days of training. It is unquestionable that many men recruited from sedentary occupations were affected by the condition before joining, although previous to that event in their life-history symptoms had never presented themselves. The question naturally arises as to what extent sedentary work actually predisposes to the affection; no conclusive answer can be returned from the data at our disposal, though they strongly suggest sedentary work as a predisposing cause. The incidence of infective disease among clerks is heavy.

"To what extent training may rid men of a predisposition to or early manifestations of the condition is also uncertain; not a few patients have related that symptoms, previously experienced, disappeared early in training to return later on active service, but the number of men who enjoy a similar early experience and endure active service without recurrence of the symptoms is unknown.

"The facts now brought forward strongly suggest that, were it possible, it would be wise in conscripting men from sedentary occupations to arrange a more thorough initial medical scrutiny and subsequently to train such as are passed for service by tenderer methods in the initial stages than those in vogue for conscripts as a whole.

"The class of military invalid with which we are dealing is a very large one; it is a very unsatisfactory one on the score of expense and time lost in training and in hospitals. It cannot be too strongly emphasized, therefore, that more than half of this class is drawn from sedentary or light occupations."

1. *Previous Disease.* Inquiry elicited the following data:

Measles	34 cases.
Rheumatism	16 "
Scarlet fever	11 "
Tonsillitis	14 "
Pertussis	9 "
Pneumonia	4 "
Diphtheria	6 "
Typhoid fever	5 "
Appendicitis	2 "
Other infections	3 "
No disease	7 "

While at first sight these figures would suggest a very direct and intimate relation between some preceding infection and the effort syndrome-complex, more careful study did not bear out this inference. The attempt was made in every instance to ascertain what the patient considered was responsible for the onset of his trouble, but in only 8 of the 50 cases could a definite cause be assigned. In 6 of these acute infection was regarded as the exciting cause, diphtheria

in 3 cases, pneumonia, rheumatism and bronchitis 1 each. The other cases started from a mental shock, 1 from the sudden death of a parent and 1 after being told at an examination for insurance that his heart was weak.

Remembering that our data refer to men examined at the very beginning of their service it is of interest and importance to compare them with those derived from men longer in service. From Da Costa the following table of antecedent conditions is taken:

ANALYSIS OF 200 CASES

Fevers (typhoid and typhomalarial)	17.0 per cent.
Diarrhea (typhoid and typhomalarial)	30.5 "
Hard field service, excessive marching	38.5 "
Wounds, injuries, rheumatism, scurvy, ordinary duties of the soldier's life and doubtful causes	18.0 "

The findings of the British Commission may be summarized thus: In 182 of a total of 558 patients examined the symptoms of the affections were first noted during convalescence from some acute infection, that is, in 33 per cent. of the cases. After further consideration of their observations they conclude that these figures by no means represent the full truth, but that in at least 50 per cent. to 60 per cent. of the cases infectious disease may be held to play the chief part in promoting the disease in its initial stages.

ANALYSIS OF 182 CASES.

Rheumatic fever or chorea	68 cases or 12 per cent. of total 558
Dysentery	14 cases or 2.5 per cent.
Typhoid fever and diarrhea	14 cases or 2.5 per cent.
Pneumonia, pleurisy and bronchitis	25 cases or 4.4 per cent.
Fever or influenza	28 cases or 5.0 per cent.
Diphtheria, scarlet fever and pus infections	33 cases or 6.0 per cent.
	— 33.0 per cent.

The role assigned to rheumatic fever in this tabulation is impressive, but they add that of the remaining 376 patients those in whom no close relation between the infectious disease and the disorder could be established at least 65 definitely belonged in the rheumatic class, although the precise significance of rheumatism in relation to the malady is in many of them uncertain.

Grouping all these observations it appears clear that no one infectious disease, or type of infection, is to be regarded as having an essential relation to the affection. During the Civil War it was the fevers and diarrheas, then prevalent, that were accused; among the British troops rheumatic fever comes to the fore, just as it does in all their health studies; with us it will doubtless prove to be infections of another type.

During the past winter we have had frequent opportunities in the

wards of the hospital to observe the influence of intercurrent acute infections in patients already subject to this affection. Under these conditions the disturbance is aggravated, convalescence is protracted and not infrequently the symptoms have become so severe and persistent as to lead to the discharge of the patient from the service.

2. *Shock*. No little interest attaches to the two cases in which the onset of the affection was attributed to mental shock, in one case the sudden death of a parent, in the other the alarm caused by the patient's being told at an examination for life insurance that his heart was weak. If the affection were a pure neurosis one would certainly expect that such experiences would play a much larger part in the causation. From the British report we learn that of their 558 cases but 13 (2 per cent.) dated the onset from shell shock or mine explosion, and that in two of this small number of cases duty was carried on until an infection sufficiently aggravated the symptoms to warrant invaliding. It would therefore appear that of the two factors antecedent infection is the much more effective in inducing the disturbances of which these patients complain.

Duration of Symptoms. Perhaps the most important finding in our own study lies in the fact that in all but one of the fifty cases the patient had suffered from cardiac symptoms for some time previous to entering the army, although in most of the cases the trouble had been aggravated by army training. Of considerable interest from the view-point of prognosis is the question of the length of time during which the disturbance had existed before the soldier's enrolment. In our series this was as follows:

Under 1 year	2 cases.
1 to 5 years	30 "
Over 5 years	12 "
Indeterminate	6 "

Without doubt the longer the condition has existed the longer the treatment required to restore the subject to normal, the more remote the prospect of ultimate success and the greater the likelihood that even if recovery occurs any new strain or new infection will cause a return of the symptoms and in the end lead to the discharge of the recruit.

Since these chronic or long-standing cases are those we at present have to deal with in our camps, and it is of the utmost importance to us to determine, so far as we may, the outlook for them and their ultimate value to the military service, it may be well to quote at length a page of the British report dealing with these problems:

"Taking all patients invalided, symptoms of the condition were present in 43 per cent. at the time the men joined the service (average duration of symptoms, nine years); 12 per cent. acquired their first symptoms on training and 45 per cent. on active service.

"Of men in whom the symptoms are acquired before joining, the

duration of training added to the stay in hospitals averages 11.3 months; the total duty performed on foreign service (light and full) averages 3.9 months. In those in whom the onset is on training the average total of training and stay in hospitals is 12.3 months; the total duty performed on foreign service averages 2.9 months. The smaller amount of foreign service completed by the men in whom the onset is on training is due to the fact that only 46 per cent. of them have seen foreign service, while of those in whom the onset was before joining 63 per cent. have seen foreign service.

"From these figures it might appear that those who have symptoms on joining are more favorable, from the military stand-point, than those who develop symptoms on training. But this conclusion is not borne out by the analysis of the categories of discharge from the hospital, for of the former 36 per cent. return to duty (10 per cent. in the full-duty category) while of the latter 52 per cent. return to duty (32 per cent. in the full-duty categories). When the onset of symptoms is on training the condition is more acute and for the moment somewhat more incapacitating, but the recovery is more rapid and more satisfactory.

"The group in which the onset is on active service a group in which the duration of symptoms is but a few months do best of all; of these 60 per cent. return to duty (35 per cent. in the full-duty categories).

"To sum up: where the disability is of long duration it is relatively mild during the initial stages of training and service; a large percentage of these men see active service abroad. But if the condition changes for the worse in these men, recovery is slower and more unsatisfactory than in those in whom a similar degree of disability has arisen more recently."

In the light of these facts it would seem questionable policy to permit any of these men who have had their disability for years before entering the army to be sent abroad; they should, at any rate, not be regarded as fit for full duty.

Other Etiological Factors. Tea and Coffee. Inquiry failed to reveal anything of significance in this relation. Seven of the fifty men used none at all, a rather remarkable return, since coffee is so regularly regarded as an essential of the soldier's diet. But one man used more than three cups of coffee during the day. Doubtless this moderation or dislike is determined largely by the results of experience, in that the men find they are more comfortable without this particular form of stimulation.

Tobacco. In view of the widespread tendency to lay the responsibility for any cardiac rapidity or irregularity at the door of Lady Nicotine, careful inquiry was made as to the use of tobacco: 7 of the 50 did not use it at all; 23 smoked very moderately; 14 used from ten to twenty cigarettes a day; 6 only admitted smoking more than twenty daily. Again, there is little question that this moderation is

dictated by experience, but it leaves no ground for assuming that tobacco plays any part of consequence in the production of the malady. The British Commission reports a like conclusion from their investigation of this subject and also quotes McGregor to the effect that the condition is as frequently found among the Sikhs, who are non-smokers, as among the other races in their armies.

Alcohol. Still more remarkable are the replies to questions on this point, tabulated as follows:

To excess	4 cases.
Moderate	21 "
Abstainers	25 "

Similarly in the British study of 454 cases 52 per cent. were total abstainers. Self-protection against unpleasant results of indulgence is probably in part responsible for this restraint, but there are doubtless many other factors. Many of the men are abstainers by conviction; many of them do not now use alcohol because it is not easily to be had. In Camp Dix intoxication was practically unknown except in the case of newly drafted men. While alcohol certainly aggravates the symptoms in these patients its use is not an important factor in the causation. This fact is rather curiously enforced by the figures in the British report, which show that in these "effort syndrome" cases return to duty are much more frequent among the heavy drinkers than among the abstainers. Relieved of the injury done by alcohol they make a more satisfactory recovery than the abstainers, who present no such *point d'appui* to therapeutics.

Symptoms. Dyspnea and precordial pain were almost constant symptoms and one or the other was given as the chief complaint in nearly all the cases. The results of our study may be shown thus:

	Present.	Absent.	Predominating.
Dyspnea on exertion	50	0	18
Pain	48	2	19
Exhaustion	43	7	4
Giddiness of fainting	47	3	1
Palpitation	49	1	8
Orthopnea or smothering at night	17	33	0

Nervousness. The patients were questioned as to whether they considered themselves nervous, and answered as follows: Very nervous, 23; somewhat, 16; slightly, 8; not at all, 3.

A glance at the table shows clearly the constancy of the characteristic symptoms. The studies both of Da Costa and the British investigators have brought out many interesting details of the several symptoms, but for our present purposes the above enumeration suffices.

Physical Signs. Heart Rate. This was taken (1) three or four minutes after the patient had entered the examining room and while he was still standing; (2) after he had been lying supine for two or

three minutes; (3) after exercise consisting in all cases in jumping up and down on one foot one hundred times. Rate per minute was here estimated on the count for the first ten seconds after the exercise was completed; (4) rate per minute estimated on a ten-second period counted one minute after exercise was completed; (5) a similar count three minutes after the completion of the exercise. It was found that there was a difference of more than fifteen beats per minute in 24 cases and less than ten beats per minute in only 12 cases. There was well-marked delay in the fall of the rate after exercise in 22 cases.

	120 per minute or over.	100 to 120.	Under 100.
Standing	19	21	10
Dorsal	4	19	27
After exercise, 1 minute	36	9	5
After exercise, 3 minutes	22	6	

Immediately after the exercise the pulse rate was tabulated thus:

	150 per minute or over.	130 to 150.	Under 130.
	25	21	4

The abnormal response to simple exercise is well shown in these tables, especially the persistence of rapidity beyond the normal period of recovery (two minutes).

Blood-pressure. This was uniformly taken with the patient sitting upright and always before exercise.

Systolic blood-pressure over 140	32 cases.
Diastolic blood-pressure over 100	7 "
Pulse-pressure over 60	16 "

The systolic blood-pressure therefore tends to be slightly higher than normal, but this rise rarely exceeds 170 mm. The diastolic pressure shows less tendency to rise above the normal than the systolic and the rise is usually less. The pulse-pressure occasionally exceeds the normal limits. In other words, while there is a tendency to modifications of the blood-pressure relations the changes in pressure are not sufficient to be of moment.

Size of Heart. This was estimated by the palpation of the apex impulse and percussion of the borders. Slight hypertrophy was noted in 19 cases; in 36 the results were normal. Meakins and Gunson report observations of peculiar interest along this line. They find the size of the heart, determined by the orthodiagram, to be normal in these cases, but they also find that in these patients exercise acts exactly as in normal individuals, confirming the findings of de la Camp, Moritz, Nicolai and Zuntz that the heart is smaller than before. These observations seem to dispose finally of the hypothesis that these soldiers are suffering from heart-strain, the results of overexercise, and that this strain has induced dilatation of the heart.

Irregularity of the Pulse. Extrasystoles were observed in 1 case, sinus arrhythmia in 9 cases and none at all in 40. It is in this category that the recent advances in the knowledge of cardiac affections enables us to work much more surely than was possible in Da Costa's day. We can say with assurance that the irregularities observed were of practically no importance and should not influence us in judging the functional efficiency of the heart or the propriety of holding the subject for service.

Deep tenderness to percussion over the apex region. This was present in 21 cases and absent in 19. Precordial areas of skin hyperesthesia were likewise present in 21 cases and absent in 19. The British Commission find that hyperalgesia is an important sign in these patients, those who have it to a notable degree showing a low capacity for work and a correspondingly poor prognosis.

Murmurs. These were observed as follows:

Systolic at apex	16 cases.
Systolic at base	2 "
Cardiorespiratory	3 "
None	29 "

None of the murmurs heard was considered as due to organic valvular disease.

It is, of course, true that there is little harmony as to what would constitute reliable criteria for a final distinction between functional and organic murmurs. In the early stages of the work these patients were regularly sent for examination with the diagnosis of mitral insufficiency or other valvular lesion. In judging the character of a murmur the history (especially of previous rheumatism), the size and action of the heart, pulse frequency and quality, blood-pressure, the location and quality of the murmur and the response to exercise were all taken into account. No part of the work of the British Commission is more striking than their conclusions as to the value of cardiac murmurs in estimating the efficiency of the heart. These are so important as to warrant their being quoted in full:

"Cardiac Murmurs. When a soldier presents the characteristic low-pitched rumbling murmur in diastole and at the apex beat, or when an early diastolic murmur, maximal at the level of the second costal cartilage, is associated with the water-hammer pulse, then, by common consent, he is unfit for duty. Instances of systolic murmurs at base or apex cannot be similarly treated. In the absence of other disqualifying signs or symptoms it is wise to entirely neglect such murmurs in soldiers. This conclusion is at variance with much current teaching and the reasons for insistence upon it are therefore given in full.

"(a) Systolic murmurs at base or apex indicate valvular disease only exceptionally; there is no conformity of opinion to the character or conduction of systolic murmurs indicating valvular lesion.

“(b) The extent of mitral valve damage which produces a systolic murmur alone is relatively slight; the disease is often limited to the valve, the heart muscle, which is the essential part of the organ, being wholly undamaged.

“(c) Patients who are invalidated on the ground of systolic murmurs alone are subsequently found when tested to be fit for service in nearly all instances. A large number of men who present such murmurs are known to have passed the most severe ordeals of active service without accident.

“(d) If a group of patients who present no murmurs and a similar group in whom systolic murmurs exist are tested in respect to their capacity for work or active service no difference is to be found in the capacity of the two groups.

“The estimate of fitness or unfitness for service can be gauged with considerable accuracy without reference to such murmurs; as soon as murmurs of systolic time are taken into consideration the issue becomes confused.”

Accentuation of the First Sound and Diffusion of the Apex Beat. The first sound was accentuated in 31 cases; in 11 the apex impulse was diffuse. The first sound was normal, with no diffusion of the apex beat in 16 cases. Diffusion of the apex beat and a forcible impulse have long been regarded as indications of hypertrophy, but the orthodiagrammatic studies made under the British Commission show them to be unreliable either as indications of the size of the heart or of its functional capabilities.

Erben's Sign. This consists in a marked retardation of the pulse-rate, when the patient squats on his heels and bends the head well forward between the knees. The pulse is first counted for fifteen seconds, the patient standing; he then assumes the squatting position and bends the head well forward; the pulse is then counted again for three consecutive five-second periods. This maneuver produces no retardation in cases of tachycardia due to febrile conditions or myocardial disease, but it is usually quite pronounced in the nervous cases. Thus in pulses averaging 120 to the minute or 10 to each five seconds the readings for the three five-second periods immediately following the assumption of this position will run: —5, 6, 7, —6, 7, 8, —6, 6, 6, etc. This phenomenon, sphygmographically demonstrable, is said by Erben to be caused by the stimulation of the pneumogastric produced by reason of the venous congestion of the brain. There are doubtless other factors in the production of the retardation, such as the increased abdominal pressure with pressure on the splanchnic nerves and vessels and possibly the indirect pressure upon the heart itself. Certainly the retardation is greater than that produced by merely lying down or even by having the patient, while lying on a bench, let the head fall as far downward over the edge of the bench as possible. Whatever the explanation it appears to be a fact that marked retardation in the Erben

position is characteristic of the "effort syndrome" cases, and is not present to the same degree, at least, in tachycardia due to organic disease. The occurrence of this marked retardation in this position has suggested that exercises involving this and similar movements might have special value in the treatment of the condition. This idea it has not yet been possible to try out.

Thyroid Gland. It has already been stated that when the diagnosis of hyperthyroidism seemed warranted it was made and the cases so classified were not included in this present series. Practically the history of the case and the presence or absence of the traditional eye signs of Graves's disease decided the group into which any questionable case should be put. Apart from the cases classed as hyperthyroidism the involvement of the thyroid was found as follows:

Slight general enlargement	11 cases.
Isthmus alone enlarged	7 "
No enlargement	32 "

Some would undoubtedly at once transfer all these cases showing any increase in size of the thyroid to the class of hyperthyroidism. That has not seemed justifiable on clinical grounds. Lewis's observations that feeding thyroid gland to the patients suffering from "effort syndrome," they react, as do normal persons and not after the manner of the hyperthyroids, would appear to settle the debate as to whether all these patients belong in the latter category.

Sweating, cyanosis of the hands and tremor of the fingers were also recorded as follows:

	Slight.	Marked.	Very marked.	Absent.
Sweating	8	25	12	5
Cyanosis of hands	12	21	3	14
Tremor of fingers	15	14	1	20

Again, these symptoms would by the radical be regarded as determining the diagnosis in the cases in which they are present, but they occur so often quite apart from any other evidence of involvement of the thyroid gland that we have been cautious as interpreting them in that sense.

Knee-jerks. The observations on this point were made with the thought that these reflexes are usually a reliable index of the tonus of the nervous system. There was a markedly exaggerated response in only 4 of the cases, a slight exaggeration in 24 and a normal response in 22 cases.

Condition of Tonsils and Teeth. In these days of tireless zeal in the search for original foci of infection no inquiry is complete without reference to the integrity of these parts. The teeth were reported as good in 31 cases, fair in 8 and bad in 11 cases.

The tonsils were found small in 30 cases, slightly hypertrophied in 10 and greatly hypertrophied in 10 cases.

Needless to say it should be regarded as of first importance to see that such handicaps as diseased teeth or tonsils should be removed, although it is not probable that such treatment will be followed by any appreciable change in the pulse rate or other symptoms in these patients.

Nature of the Affection. This is still a moot question. Da Costa regarded it as an irritability of the heart, maintained by a disordered nervous system, but could go no further in his explanation of the symptoms. In the light of our present conceptions of physiology and pathology some suggest hyperthyroidism, others increased adrenal activity as the explanation of the phenomena. Bacteremia has been suggested but not proved. Reviewing these various opinions the British Commission inclines to the belief that the disturbance may be a chronic toxemia or disturbance of metabolism, the result possibly of a previous infection, but find many difficulties in frankly committing themselves to this hypothesis. It may fairly be said that we at present have no knowledge of the causations of the disease which determines clearly the therapeutic measures to be applied to it. As the results of his experience Da Costa put special value upon rest and digitalis. The British Commission find both these measures useless and possibly harmful. They advocate progressive physical training and lay out a carefully graded system of exercises through which the patients are passed. We have as yet no sufficient experience of our own and must for the present follow the lines of procedure laid down as the result of their careful study of many hundreds of cases. It may only be surmised that Da Costa's conclusion in favor of rest and digitalis sprang from the fact that he had included among his cases a sufficient number of instances of auricular fibrillation to influence his judgment of the entire group. He notes that digitalis failed of effect in many cases.

The inferences drawn from this study may be summarized as follows:

1. The irritable heart or effort syndrome cases constitute a symptom-complex rather than a definite disease. It seems clear there is no definite disease of the heart, and we agree with Lewis that it is highly desirable to avoid any terminology which suggests that there is.

2. The affection is not peculiar to soldiers but often precedes entry into service, though it may be exaggerated or in some cases produced by the active exercise or vicissitudes of the military life.

3. Occupation in civil life is as much a result as a cause of the disturbance, in that men who know their weakness usually adopt an employment suited to it.

4. In the great majority of cases no definite cause of the disorder is ascertainable. When such can be found it is most often an acute infection.

5. Tobacco, alcohol, coffee and tea, though possible causes of aggravation of the symptoms, cannot be regarded as prime factors in the causation.

6. Hyperthyroidism is suggested in some of the cases, but if present it is in a mild degree, and there seems no valid ground for regarding it as more than a contributory factor.

7. In the light of the experience now available in the studies of Da Costa and the British Commission it would seem wise to retain many of these patients in the hope of rendering them fit for duty of some kind. In view of their very limited usefulness in foreign service they should not be sent abroad.

8. For the present, at least, the line of treatment must be that of progressive physical training as laid down by the British Commission, which, even if it fails to produce satisfactory therapeutic results offers the best means of classifying the men as to their physical ability to perform military service.

**CLINICAL REPORT UPON CASES OF LOBAR PNEUMONIA
TREATED WITH ANTIPNEUMOCOCCUS SERUM AS
OBSERVED AT GENERAL HOSPITAL NO. 6, FORT
MCPHERSON, GEORGIA, OCTOBER, 1917,
TO MAY, 1918.**

BY LIEUT.-COLONEL C. N. B. CAMAC, M. C., U. S. A.,
NEW YORK.

THIS report deals especially with cases which were diagnosed clinically, bacteriologically and by postmortem as lobar pneumonia due to the pneumococcus. Reference is made to cases which were given antipneumococcus serum but which at autopsy were shown not to be lobar consolidation. There are added also cases of infection with streptococcus hemolyticus, but these are included by way of contrast only, our conclusion being that cases of pneumococcus infection present clinical features quite different from those of streptococcus infection. Streptococcus may be, and frequently is, superimposed upon the pneumococcus or may occur separately. Whether separate or in conjunction with the pneumococcus we believe that the clinical features are differentiable in the majority of cases.

We have looked upon the mixed infections as similar to the complicating infection of pyogenic organisms in typhoid or smallpox. Moreover, we have felt that bronchopneumonia should not be considered as having anything to do with lobar pneumonia any more than the tuberculous ulcer of the intestine should be considered in connection with typhoid ulcer except to show the difference. The pneumococcus infection of whatever type when treated at the outset

with serum, in our experience, does well. When treated late it assumes all the serious features with which we were familiar before serum was used when the mortality ranged from 20 to 50 per cent. From bacteriological findings we have concluded that those cases which were treated late became, through the action of the pneumococcus, fertile soil for the pyogenic organism or at least reduced the resistance to such an extent that the pyogenic organism found non-resistant soil in which to flourish. We have been unable to demonstrate whether these pyogenic organisms were previously lodged in the individual, in the throat, for example, or whether they gained access during the pneumococcus infection. We have on meager evidence inclined to the former. The serious pulmonary sequel to measles, which is so fatal in military hospitals, we have considered as a disease distinct and separate from the pneumococcus lobar pneumonia. In our experience the pneumococcus has been an extremely rare complicating infection in measles. I will not consider further this pulmonary complication of measles, for it is so different clinically, anatomically and bacteriologically that it belongs to a separate discussion. The report of "pneumonia" as a complication or cause of death in measles should be abandoned as incorrect and misleading. The Surgeon-General's Office has adopted the term "measles pneumonia," but we believe that the term "pneumonia" should not be used at all in this connection.

From the statistics of the Rockefeller Hospital and from the review of our 139 cases we feel that the pneumococcus pneumonia when treated with the serum early is a comparatively mild infection. I would like to repeat that this report deals with those cases which show, clinically, consolidation of part or of an entire lobe of the lung and due to the pneumococcus.

SUMMARY OF CASES.

I. PNEUMOCOCCUS ALONE.

Type uncomplicated.	Incidence.	Recoveries.	Deaths.	Mortality. Per cent.
Type 1	26	25	1	3.8
Type 2	18	17	1	5.5
Type 3	10	10	0	0.0
Type 4	27	27	0	0.0
Total	81	79	2	2.4

It is noteworthy that the two fatal cases were colored and both worked as stevedores. Nephritis complicated the pneumonia in both cases, the one of chronic type the other an acute nephritis developing during the height of the disease. Each received large doses of serum on and after the fifth day of the disease. At necropsy each showed the characteristic lobar consolidation and the evidence of nephritis in addition.

II. PNEUMOCOCCUS AND STREPTOCOCCUS.				
	Incidence.	Recoveries.	Deaths.	Mortality. Per cent.
Type 1	3	2	1	33.0
Type 2	0	0	0	0.0
Type 3	0	0	0	0.0
Type 4	2	1	1	50.0
Total	5	3	2	40.0
III. STREPTOCOCCUS ALONE (Hemolyticus or Viridans).				
	11	5	6	54.0
IV. UNDETERMINED (Not Pneumococcus or Streptococcus).				
	39	38	1	2.2
V. MISCELLANEOUS.				
Pneumo Type 1 and 2	1	1	0	0.0
B. influenza	1	1	0	0.0
Staphylococcus in throat	1	1	0	0.0
Grand total	139	128	11	7.9

METHOD OF PROCEDURE. Immediately upon the finding of clinical signs indicating an area of consolidation the patient is desensitized with polyvalent antipneumococcus serum (Mulford's) and placed in a pneumonia ward, where the following instructions are posted and strictly adhered to:

INSTRUCTIONS—MEDICAL SERVICE.

INSTRUCTIONS TO THE MEDICAL STAFF REGARDING ALL CASES OF LOBAR PNEUMONIA.

“1. Isolation: Caps, gowns and gauze mouth guards for attendants, nurses and doctors. Sheets between beds and mouth guards for patients leaving bed.

2. Sputum: (a) Collect sputum in sterile bottles and send to the pathologist at the clinical laboratory for transmission to the department laboratory. (b) Laboratory slip marked as follows must accompany the sputum. ‘Sputum for determination of pneumococcus type.’ (c) The specimen must reach the department laboratory within four hours after it has been expectorated.

3. Urine: Collect 6 ounces of the twenty-four hours' specimen in sterile bottle and send to the pathologist at the clinical laboratory for transmission to the department laboratory. A laboratory slip marked as follows must accompany the specimen: ‘Urine for Pneumococcus Differentiation.’

INSTRUCTIONS FOR SUCH CASES OF LOBAR PNEUMONIA AS ARE TO RECEIVE SERUM TREATMENT.

Desensitizing: (a) Administer 2 c.c. of serum subcutaneously and at two hours' interval administer the following amounts: 3 c.c. and 5 c.c., a total of 10 c.c. After each administration look for signs of hypersensitiveness, such as: (1) Difficulty in respiration. (2) Cyanosis. (3) Violent coughing. (4) Sense of restriction about chest. (5) Marked variation in pulse. In case these occur give same dose as previous one at the end of two hours' interval. (b) From two to four hours after the last desensitizing dose, administer the balance of the 100 c.c. intravenously. (c) Administer 100 c.c. intravenously every twelve hours. The intravenous administration of serum, warmed to body heat, should be by gravity, and very slowly. In case of signs of hypersensitiveness, as noted above, occurring during the administration of serum, stop the serum at once.

Serum Sickness. This is not a serious condition and does not contraindicate the continued administration of serum, though it is due to the serum.

The manifestations are fever, itching and redness of skin, urticaria. This condition is entirely different from true anaphylaxis, which in mild form would be manifested by the symptoms of hypersensitiveness noted above and which in severe form may be rapidly fatal."

In the early part of the winter our laboratory facilities were inadequate and it required considerable time to get a report on the sputum from the department laboratory, four miles away. This inadequacy still exists on account of the difficulty in procuring mice and the need of a larger laboratory and staff of laboratory workers. The patients, however, did not suffer in consequence, as the polyvalent serum were administered without waiting for laboratory findings. If the report Type I was returned the patient received Type I serum, otherwise the polyvalent serum was continued. The polyvalent serum used has been prepared according to Mulford, so as to prevent the neutralizing of the Type I element, so that in giving the polyvalent serum, Type I, in full strength is being given, if Mulford's claim is correct. We have no proof of this beyond our clinical results. We believe too that by using the small doses to desensitize the patient is better prepared for the larger doses and the danger of anaphylaxis is minimized. We have preferred the subcutaneous to the intradermal method because with the varying personnel in a military hospital we consider it safer to desensitize than to attempt to ascertain the sensitiveness of the subject with possible grave errors in judgment. Even with the trained observers at the Rockefeller Hospital such errors in judgment are reported by Cole.¹

¹ Ref. monograph Acute Lobar Pneumonia, Rockefeller Institute, No. 7, October 16, 1917, p. 63.

Clinical Features. The three striking features have been: (1) Variations in temperature. (2) The rapid recovery. (3) Absence of profound toxic effects.

The rapid breathing, flushed face and further manifestations of profound toxemia have been absent in the majority of our cases unless complicated by some other septic organism. A careful inspection of our temperature charts fails to reveal any uniformity of the lobar pneumonia curve. Invasion by another organism is usually accompanied by a greater variation in the curve, but a number of the cases in which no other organism could be demonstrated have shown a temperature decline with a step like lysis similar to that of typhoid but without the long typhoid period of decline. Extension of the pneumonic process or involvement of another lobe is marked by a sharper and more sustained rise, whereas invasion by another pyogenic organism presents a more gradual rise and shows greater variations. About 5 per cent. of the cases show the sustained temperature with the sharp critical fall commonly described as characteristic of the pneumonia curve. The leukocyte count, beyond indicating a good prognosis when high, has been no guide as to the development of complications or extension of the process.

Complications. Empyema and otitis media have been the most frequent. The former of these will be dealt with in a separate report. Two cases presented pneumococcus abscesses of the abdominal wall. Streptococcus pericarditis occurred in two cases. Mediastinal abscess in one case. Meningitis in one case only. This case will be described under the Fatal Cases. Acute nephritis occurred in about 15 per cent., as evidenced by albumin and casts in uncomplicated cases; 75 per cent. in complicated cases.

Serum Treatment. The amounts of serum administered have varied between 50 c.c. and 600 c.c., with an average of 250 c.c. About 10 per cent. of the cases did not require serum treatment. In the military service it is possible to begin the serum treatment much earlier than in civil practice. Few of our cases have come under treatment later than the third or fourth day, and many of them have been treated in the first forty-eight hours. Treatment was begun on the first clinical sign, without waiting for differentiation of type. For this purpose polyvalent serum was used. If the case showed Type I this serum was used, otherwise polyvalent serum was continued. No systematic blood cultures were made on our cases, but from the Rockefeller report² and from our low mortality we concluded that the early administration of serum prevented the development of or cleared the blood of pneumococcus organisms. In the few cases in which blood cultures were made this conclusion was supported. The rapid recovery of between 50 and 60 per cent. of all cases would indicate that the

² Monographs of the Rockefeller Institute for Medical Research No. 7, October 16, 1917, p. 79.

early use of serum tends to diminish the frequency of the complications.

Preventive Treatment. Dichloramin-T in chlorcosane 2 per cent. was used as a throat spray for attendants and with some of the cases. With the measles cases we found that pulmonary complications were less frequent when this treatment was employed.

Serum Sickness. About 50 per cent. of the cases showed signs of serum reaction. These ranged from simple erythema to the extensive urticaria, with general swelling and joint pains. Some of the severer cases developed after 50 c.c. of serum had been given and others showed no reaction after 400 to 600 c.c. Manifestations appeared from twelve hours to fourteen days after administration. Only 2 cases showed any alarming features. One of these had blood and blood casts and excessive amount of albumin in the urine. The other, who received only 50 c.c. of serum, with prompt fall of temperature which remained normal, two weeks later developed general swelling, making him unrecognizable, together with swelling and pains of many of the large and small joints and with albumin and hyaline casts in the urine, all of which disappeared in five or six days. In some of the cases we have endeavored to determine whether a mononuclear increase in the blood would indicate a serum rise of temperature, as suggested by Cole, but we found no uniformity in this from which conclusions could be drawn.

Anaphylaxis. Only 1 case presented symptoms of anaphylaxis. This was a case of asthma of unknown cause. In desensitizing him he showed no reaction, but when 80 c.c. of serum had been administered, cyanosis, dyspnea with asthmatic breathing, cold sweat, disturbed, rapid heart action and general signs of collapse developed. Administration of serum was continued up to 100 c.c., and subcutaneous injection of adrenalin was given. In twelve hours the temperature was normal and continued so, requiring no further treatment.

Streptococcus Infection Alone and Complicating Pneumococcus. Reference to the Table will show the frequency of these conditions. We have not practised streptococcus vaccination. With the accumulation of evidence it is becoming more and more apparent that when this organism is added to pneumococcus infection the case assumes grave features. To combat this added infection we are preparing to carry out immunization with streptococcus vaccines. This measure has been resorted to in some of our base hospitals and is suggested by Cole and MacCallum in a recent communication.³ The destructive power of the streptococcus is well demonstrated in the pulmonary complication of measles, in which the pneumococcus is rarely found. In reviewing the records one is disposed to conclude that it is the streptococcus, superimposed upon pneumococcus, that gives lobar pneumococcus pneumonia its real virulence. Early

³ Jour. Am. Med. Assn., April 20, 1918, No. 16, lxx, 1151.

treatment with serum seems to lessen the tendency toward the development of this mixed infection. While slight tinging of the conjunctiva is common in this disease we found marked jaundice of the conjunctiva in those cases of streptococcus infection alone or complicating pneumonia.

Other Treatment. Diet: While this is a comparatively brief febrile disease we have felt it advisable to maintain a diet of about 2000 calories, consisting of easily digested fluids and semisolids; 3000 c.c. or more of water a day is routinely given. Whisky has been given when indicated.

Heart Stimulants: We have in most cases followed the advice contained in the Rockefeller monograph, namely, digitalizing early. We have used Merck's digipuratum tablets, $1\frac{1}{2}$ grains each. One such tablet given three times a day for *three days*. Strychnin was not given.

Abdominal Distention: This has been an infrequent feature. In 3 of the cases peritonitis was suspected and was found at autopsy in 1 of these. By the use of oil and turpentine stupes, enemata and by the regulation of diet the distention was relieved in most cases.

Open Air: For the greater part of the winter, patients were moved to verandas and allowed to remain there from 11 A.M. to 4 P.M., protected by screens. (Lobar cases only.)

IMPORTANT POINTS. 1. Early diagnosis is essential.

2. Clinical signs of consolidation should be followed by immediate use of polyvalent or other serum.

3. If more than 250 c.c. of serum are required and the temperature and toxic signs continue, complication by other organism should be suspected; like malaria when treated with quinin the pneumococcus is rapidly overcome by serum.

4. Uncomplicated pneumococcus infection is a comparatively harmless and rarely a fatal condition.

5. The colored men are more susceptible, possibly because they keep up and about longer and come under treatment late. Their complaints may be disregarded by officers who think them shirking.

6. Leukocytes are not a reliable guide in determining the added streptococcus infection. Mononuclear increase is not a guide in determining serum temperature rise from septic temperature.

7. Protective streptococcus vaccination should be employed.

8. Diet: 2000 calories; 3000 c.c. of water should be administered daily.

C. N. B. CAMAC, Lieut.-Col., M.C.,

Chief, Medical Service.

WILLIAM L. VROOM, Major (now Lieut.-Col.), M.C.,

Ward Surgeon.

HENRY K. STINSON, Major, M.C.,

Ward Surgeon.

A. J. ROSENBERG, Captain, M.C.,

Ward Surgeon.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE,
MARYLAND,

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF
CINCINNATI, CINCINNATI, OHIO,

AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

Clinical Significance of the Abnormally Wide Ventricular Deviation in the Electrocardiogram.—NEUHOF (*Arch. Int. Med.*, July, 1918). The author has noticed in cases of myocardial disease (hypertension, aortitis, precordial distress, decompensation) that electrocardiographic tracings show an abnormal width of deviation of the *R* wave of the ventricular complex. Taking 0.07 of a second as the lower limit of abnormal he shows that all of his tracings with abnormally wide *R* presented unmistakable signs of myocarditis. "It had no relation to the height of the *R* wave, pulse rapidity, cardiac rhythm or to the underlying disease producing the myocarditis. In some of the cases severe decompensation was present; in others, absent. Though no definite statement of the fundamental cause of the abnormally long duration of the *R* phase can be offered, its frequent association with myocarditis would make it appear possible that this lesion acted as a direct hindrance to the proper, normal, rapid prolongation of the wave of electrical excitation through the ventricular musculature."

Studies on Renal Function during and Immediately Following Some of the Acute Infectious Diseases.—FROTHINGHAM (*Arch. Int. Med.*, July, 1918). Cases selected for this study were among young people who presented no urinary evidence of chronic or acute nephritis. The series included 6 cases of typhoid fever all on high caloric diet, 4 cases of pneumonia Group I (Cole), 6 cases of pneumonia Group IV (Cole),

5 cases of acute articular rheumatism and 6 miscellaneous cases (diphtheria, gonorrhoeal arthritis, periosteal abscess, acute gout). Renal function was studied during and just after the infection by (a) phenol-sulphonephthalein test, (b) the estimation of blood urea and (c) the determination of McLean's index of urea excretion. The author concludes: "From these studies it may be concluded that these tests for renal function, namely, the phenolsulphonephthalein elimination, the urea nitrogen in the blood, and the index of urea elimination, failed to show consistent evidence of impaired renal function during the course of or following these acute infections in which the clinical picture or the urinary examination by the older methods showed nothing suggestive of acute nephritis."

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE
UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL
HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Pleural Infection in Wounds of the Chest; Pleurectomy for Old Suppuration with Pachypleuritis.—ROUX-BERGER and POLICARD (*Lyon Chirurgial*, 1917, xiv, 969) say that at the present time, wounds of the pleura and lung are more complicated than ever because of the serious infections from refraining from surgical aid altogether or from inadequate operations. In the treatment of lung wounds we must admit, as a fundamental basis, the theory generally accepted in war surgery: that these wounds are all infected; that it is easy to prevent infection by fully operating at once; that it may be extremely difficult to treat and sometimes impossible to cure an advanced pleuropulmonary infection. The treatment ought to be applied systematically to all chest wounds by shell splinters or bullets. It should be thorough and early and comprise the following stages: (1) A complete removal of the fractured rib, the infection of which, close to the pleura, is the chief cause of purulent pleurisy following these wounds. (2) A systematic extraction of the projectile whether it be in the pleura or in the lung, only very small projectiles or those situated very far from the opening may be disregarded. (3) The lung must be sewed up and the wound caused by the operation completely closed. Notice how restricted surgical aid on the lung is, for we cannot possibly remove all the bruised tissues. When this preventive treatment has not been applied we shall see pleuropulmonary lesions develop, clinically characterized by rapid cachexia and anatomically characterized by a noticeable thickening of the pleura, also by the constriction of the lung into a hard envelope and also by lesions in the lung of the acute bronchopneumonia type. The treatment of these deep-seated lesions is: (1) The removal of the infected fractured rib, which has been either totally neglected

or else wrongly treated. (2) The previous draining and disinfecting of the pleural cavity. (3) The removal (this as extended as possible) of the parietal pleura. (4) The decortication of the parietal and visceral pleura. In certain cases when the infection of the pleura does not extend to the top of the thoracic cavity the suppurating mass might be taken away whole. When these large pachypleural lesions have been taken away, the most serious obstacle to a cure will have been got rid of: but, the fresh cavity in the pleura will have to be constantly drained and must be looked upon as still infected.

Mixed Tumors of the Salivary Glands.—FRASER (*Surg., Gynec. and Obst.*, 1918, xxvii, 19) says that the mixed tumors arise from the ducts of adult glands. No claim is made that true neoplasm has been experimentally produced but the experimental results justify the conclusion that the primary structures of the mixed tumors may easily arise from the ducts of the adult gland. Facts established from the morphological study of 14 mixed tumors prove the point. The endothelial theory has no foundation in fact. All the so-called endothelial structures are easily explained as natural modifications of primary duct formations. Injury such as localized or partial obstruction of ducts probably plays a prominent part in the origin of these tumors. The most common precursor of cancer of the breast, chronic cystic mastitis or diffuse fibroadenomatosis, is a condition very similar to that which can be produced in the dog's submaxillary gland. Fraser has reproduced this condition with morphologically cancerous transformation in a series of experiments on the mammary glands of animals. The cartilage is developed from the epithelium of the parenchyma of the tumor.

Transfusion with Preserved Red Blood Cells.—ROBERTSON (*British Med. Jour.*, June 22, 1918, p. 691) describes in detail and gives the results of his method. There is a definite need in front area medical work of a method of giving transfusions rapidly. The difficulty of procuring sufficient blood under rush conditions, the time consumed in carrying out the transfusions, and the need of every available medical officer in the operating theatre, all tend to reduce the number of transfusions which can be given. The use of preserved human blood cells for transfusion suggested itself as a possible solution of certain of these difficulties. A quantity of blood sufficient for a number of transfusions could be stored up beforehand and used as needed. The technic of transfusing such blood is simple and could be handled by one medical officer. It is possible to preserve living human red blood cells for several weeks in a solution of dextrose and citrate when kept at ice-box temperature. This method has been made use of for giving transfusions at casualty clearing stations during a rush period. A quantity of blood was stored up beforehand ready for use when needed. The blood was kept for varying periods up to twenty-six days before transfusion. Twenty-two transfusions were given to twenty cases by this method, the majority of which were hemorrhages. The results were quite as striking as with blood freshly drawn. No apparent harmful effects were observed, as reactions or evidence of increased hemolysis after transfusion. Experiments in the transportation of preserved blood have shown that it can be carried a considerable distance without injury.

Abuse of Drainage Tubes.—HATHAWAY (*British Med. Jour.*, June 29, 1918, p. 718) says that as a result of our war experience wounds of the head, chest, abdomen (even with fecal contamination) and knee and other joints are sewed up with impunity after early and complete operation, and the results are excellent. To replace a drainage tube all that is necessary is to put something into the tissues which will keep a "passage" open but which does not leave an open "drain." A soft piece of folded rubber, for instance, in an appendix abscess, will allow pus to come away but will not leave an open "drain" by which secondary infection of staphylococci, from the skin, or other organisms can gain entrance. The two main principles of civil surgery taught by the war are: (1) Early and complete operation, and (2) that secondary or mixed infection is worse than primary infection. In a severe case of pneumococcic empyema, Hathaway excised a piece of rib under a local anesthetic and made a small incision into the pleura. On emptying the pleura the cavity was washed out with flavine and about a pint of a suspension of iodoform in paraffin was injected, after which the wound was tightly closed by sutures. His general condition at once improved, the pulse and temperature gradually dropped and he made a better recovery, in all probability, than with an open "drainage tube." Hathaway concludes that in order to avoid mixed infections surgeons must practice primary suture far more than in the past, and completely give up the use of rigid open drainage tubes. If a secondary abscess or leakage from bowel should occur it will be dealt with by the inherent resistance of the body to infection, or should an abscess form it can be treated by a second operation, after adhesions have formed.

New Pathology of Syphilis.—WARTHIN (*Am. Jour. Syphilis*, 1918, ii, 425) says that the gumma is not the essential lesion of old or latent syphilis. It is a relatively rare formation and the great majority of cases of syphilis run their course without the formation of gummatous granulomata. The new pathology of syphilis is based upon the demonstration that the essential tissue lesion of either late or latent syphilis is an irritative or inflammatory process, usually mild in degree, characterized by lymphocytic and plasma-cell infiltrations in the stroma, particularly about the bloodvessels and lymphatics, slight tissue proliferations, eventually fibrosis and atrophy or degeneration of the parenchyma. These mild inflammatory reactions are due to the localizations in the tissues of relatively avirulent spirochetes. Syphilitic inflammations of this type occur in all tissues and organs, but are easily recognized in the nervous system, heart, aorta, pancreas, adrenals and testes. They are, however, usually widely distributed throughout the entire body, although in individual cases showing special predilection for certain organs or tissues. No explanation for these system, organ or tissue predilections is yet evident; neither is there any explanation of those cases in which all organs and tissues show the most severe degree of these lesions. The syphilitic is a spirochete carrier. In this respect the *Spirocheta pallida* is to be classed with the trypanosome, the malarial organisms, lepra and tubercle bacilli, streptococcus, etc. Syphilis tends to become a mild process, but at any time the partnership between the body and the spirochete may become disturbed and tissue susceptibility

or virulence of the spirochete become increased so that the disease again appears above the clinical horizon. Immunity in syphilis depends upon the carrying of the spirochete. A price is paid for this immunity in the form of the defensive inflammatory lesions previously described. The disastrous effects of syphilitic infection usually require a period of years for their development. The slow progressive lesions, fibrosis and atrophy, may at last manifest themselves in paresis, tabes, myocarditis, aortitis, aneurysm, diabetes, hepatitis or in many forms of tissue damage and functional disturbance. Lesions of the viscera are much more common and important clinically than those of the central nervous system, but they are rarely recognized as syphilitic by the clinician. Syphilitic death occurs most frequently in males between the ages of forty and sixty years. Chronic myocarditis is the most common form of death due to syphilis. The pathological diagnosis of syphilis is essentially microscopic. Only in a relatively small number of cases are the gross lesions (tabes, gumma, aortitis, etc.) typical enough to be recognized by the naked eye. A negative diagnosis of syphilis cannot be given with any certainty without a routine microscopic examination of all organs and tissues, but particularly of the left ventricle wall, the aorta, both its arch and abdominal portion, the testes, pancreas and adrenals.

Intravenous Injections of Sodium Iodide in Massive Doses in Obstinate Syphilis.—HOWARD (*Am. Jour. Syphilis*, 1918, ii, 550) bases his study upon a laryngeal case which received 125 massive doses of iodide, 54 salvarsan and many hundred intramuscular mercury injections. The indications for intravenous iodide treatment are as follows: Whenever the full iodide effect is required; when iodism develops before the desired result is obtained, iodide may be continued intravenously; in unconscious patients or those unable to swallow; in late internal syphilis, tabes, paresis, cirrhosis of the liver, aortitis, etc.; when mouth medication fails to be effective and symptoms progress. It is doubtful if there are any contraindications except lack of positive indications. He concludes that sodium iodide intravenously is harmless, and undoubtedly superior to both the potassium and the sodium salt given by the mouth. It contains relatively more iodine than the potassium salt. Sodium iodide can be given in much larger doses than the corresponding potassium salt and is not depressing to the heart muscle, as is the case with the potassium iodide. It is better tolerated intravenously than by mouth and can be given in larger doses. The treatment is administered daily. Patients often prefer the intravenous mode of administration. A solution of from 5 to 10 per cent. strength is correct and its injection painless. No reaction appears until large doses are reached and iodism is rare. Intravenous dosage is 10 to 335 grains. Chills started at 225 grains and have been reported by no other observer.

Gunshot Wounds of the Peripheral Nerves.—NOON (*Lancet*, July 27, 1918, 100) between June, 1915, and March, 1918, observed 250 cases in the Norfolk War Hospital. He concludes that the diagnosis of an injury to a peripheral nerve ought to be made at the earliest possible time; successful recovery depends upon early, correct and continuous

treatment; primary suture should be considered and practised whenever possible; that there should be no unnecessary delay in exploring a nerve if there is sufficient evidence that it has received some injury resulting in a macroscopic pathological lesion; it is almost certain that some macroscopic lesion is present in cases which show no signs of recovery after four months' treatment; that operations on injured nerves should only be done in well-equipped general hospitals and by those surgeons who have ample experience of such cases; that sufficient attention is not paid, usually to the early preoperative and postoperative treatment and that paralytic deformities and shortened muscles are often the result of ignorance and neglect; that the extreme gravity of an injury to a peripheral nerve is not sufficiently realized by the general practitioner.

Empyema in Base Hospitals.—The Surgeon-General's Office (*Review of War Surgery and Medicine*, August, 1918, No. 6, i, 1) reports the results of a study of empyema in base hospitals by a commission appointed for the purpose. The commission reached the following conclusions: An exudative pleuritis is a relatively frequent complication of bronchopneumonia associated with hemolytic streptococci. The evidence that this complication is an example of selective invasion of serous membranes by this organism is defective. The involvement of the pleura is probably an extension of the infection from the lungs, often through the medium of a subpleural pulmonary abscess. During the early stages of the pleuropneumonic process the pleuritis is probably of far less import than the pulmonary condition and general toxemia. The evacuation of the pleural exudate by operation early in the disease involves greater risks, without compensating benefits, than the removal by aspiration. Much of the relief offered by operation without its attendant dangers can be offered by aspiration, repeated according to indications. The condition of the patient at this time calls for medical rather than surgical treatment. The results of further immunological studies may offer a mode of treatment particularly applicable to the early phases of infection with the hemolytic streptococcus. At present there is little or no evidence that available sera are useful. In the early stages of this pleuritic infection the exudate is serofibrinous, the amount of serum being often very large. Later, the exudate becomes progressively more purulent and eventually is a frank, creamy pus. If treatment by aspiration is continued thereafter this pus may become sterile, as has been observed in one case. But this should be regarded only as an unusual occurrence and for a rapid convalescence an operation for its removal and access to the cavity for drainage and antiseptic treatment is called for. Three of the cases, however, have recovered, with repeated aspirations, without the necessity of operation. But in none of these had frank pus formed by the time of the last aspiration. During the period in which the above changes in the pleural fluid are taking place the general condition of the patient usually improves and operative interference is attended with comparatively little risk and much benefit. The operation should be preceded by a fluoroscopic examination to fix upon the most favorable site for the incision. Local anesthesia suffices and is preferable to a general anesthetic. The drainage of the empyemic

cavity should be both complete and continuous. Antiseptic treatment of the cavity should be instituted as promptly and thoroughly as conditions permit. In cases not complicated by bronchial communications with the empyema cavity a neutral solution of sodium hypochlorite, 0.5 per cent. (Dakin's solution), may be used effectively in cleansing and disinfecting the cavity. In recent cases, with free access to all parts of the cavity, dichloramin-T, 5 per cent., dissolved in chlorcosane, may be substituted for Dakin's solution; but if there is a thick fibrinous deposit upon the pleural surfaces this is less readily removed and drainage more difficult to maintain than when Dakin's solution is employed. In applying chlorin antiseptics (Dakin's solution or a chlorcosane solution of dichloramin-T) the following conditions should receive attention: free drainage; contact of the solution with all parts of the cavity, which is best attained by the use of Carrel tubes; adequate quantities of the solution must be used with sufficient frequency to maintain its action over the period of time necessary for disinfection; the progress of disinfection may be followed by bacteriological examination of the discharges; when the empyemic cavity has become cleansed beyond the point characterized by a viscid secretion from the wound there is usually evidence of increased freedom for expansion of the lung; the danger of such cicatricial fixation of a compressed lung is an indication for prompt operation and cleansing of the empyemic cavity after the acute stages of the disease have passed; expansion of the lung can be encouraged and perhaps accelerated by various procedures, such as (1) blowing against resistance; (2) the use of negative pressure and gentle suction devices; (3) properly controlled exercises which induce not only a more active metabolism but also more active breathing; the influence of such measures can be directly observed, but unless they can be maintained over a period at least long enough for agglutination between the surfaces to take place it is doubtful whether they materially hasten obliteration of the pleural cavity. For roentgen-ray examination of old cavities with fistulas it has been found that the thorium nitrate in 10 and 15 per cent. solution is satisfactory; its advantages over pastes of various kinds are its ease of introduction and of withdrawal.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

Etiology and Treatment of Pruritus Ani.—Out of 181 cases of pruritus ani examined, MURRAY (*Jour. Am. Med. Assn.*, 1918, lxxi, 1449) found *Streptococcus fecalis* present in 168. Examination of the blood of every patient showed that the coefficient of extinction of opsonins for *Streptococcus fecalis* was low, while in patients suffering from rectal

diseases without pruritus it was normal. Whether the infection occurred because of the low opsonic index or whether the opsonins were lessened because of the invading organism was not determined. Murray treated these cases by means of an autogenous vaccine. Of 113 cases treated in this manner, distinct relief was obtained in 99. Thirteen patients received little or no benefit, but only 4 of these received a sufficient number of treatments. Murray concludes that pruritus ani is caused by an infection by one of the streptococcus group or associated with it. This infection may be primary, secondary or the aggravating cause. Statistics of 4000 distinctly rectal cases show that only about 10 per cent. had pruritus ani, which is, he thinks, sufficient evidence that the appearance of pruritus in these conditions is merely coincidental. Murray believes that pruritus ani will not be improved by operative measures unless the phagocytic power of the blood be increased, and states that a relapse may be expected if the opsonic index of the blood is again lowered enough to allow a reinfection.

Treatment of Influenza Pneumonia by the Use of Convalescent Human Serum.—MCGUIRE and REDDEN (*Jour. Am. Med. Assn.*, 1918, lxxi, 1311) found the mortality from pneumonia following influenza at first as high as 50 to 60 per cent.; later dropped to 30 per cent. Over 400 cases were treated at this naval hospital. Thirty-seven cases in all were treated by serum. Of these, 1 died, 30 are convalescent and 6 are still under treatment, all but 1 of whom have a favorable outlook. The serum was obtained from convalescent patients. The most beneficial results were obtained when the serum was given within the first forty-eight hours of the pneumonia complication. The dose of serum administered was from 75 to 125 c.c. intravenously, the majority of patients receiving about 300 c.c. The treatment was continued until there was no doubt about the recovery of the patient. If results from a serum were not obtained in the first twenty-four hours after its use the serum from another donor was used. Persistent attempts were made to test the potency of the serum of the donors by complement-fixation and by gross agglutination, using the influenza bacillus as an antigen; but so far the writers have found no method of testing the antibody content of the serum except by its clinical action. They conclude that, even making allowance for the lessened virulence of the organism at the time of observation, the serum from convalescent influenza pneumonia patients has a decided influence in shortening the course of the disease and in lowering the mortality.

Serum Treatment of Type I Pneumonia Occurring in Association with an Epidemic of Influenza.—During the epidemic of influenza at Camp Devens, pneumonia clinically atypical from the classical acute lobar pneumonia became very prevalent. A small number of these were demonstrated to be due to *Bacillus influenzae* alone. Of the patients showing clinical signs of pneumonia the usual percentage (20 per cent.) of Type I pneumococcus was demonstrated in the sputum. SPOONER, SELLARDS and WYMAN (*Jour. Am. Med. Assn.*, 1918, lxxi, 1310) report briefly the effect of Type I serum in these cases. Before the epidemic, serum of low titer was used in the treatment of typical

Type I lobar pneumonias. In this group there was a mortality of 20 per cent. During the epidemic, with essentially the same treatment, there was a mortality of 43 per cent. At the height of the epidemic a supply of high titer serum was obtained. This was administered to 15 patients, 14 of whom recovered—a mortality of 7 per cent. The patient who died was in an extremely critical condition at the time of administration of the serum. An unusually high mortality (50 per cent.) in Type II cases of pneumonia was found during the influenza epidemic. The writers conclude that it is inadvisable to inject pneumonia patients with large quantities of low-grade serum.

The Rat and Poliomyelitis.—From the experiments here reported, AMOSS and HASELBAUER (*Jour. Exp. Med.*, 1918, xxviii, 429) conclude that it is improbable that the rat acts in nature as the reservoir of the virus of poliomyelitis.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Cesarean Section for Eclampsia.—INGRAM (*Am. Jour. Obst.*, June, 1918) reports the case of a patient weighing about 200 pounds admitted to the hospital in convulsions and semicomatose. She was a primipara, aged thirty years. On vaginal examination the cervix was long and firm, the vagina very long and small, so that the presenting part could be felt with difficulty. During one and a half hours after admission she had five severe convulsions, and Cesarean section was immediately performed. It was found that the patient had twins. Both children were dead at delivery. The patient's convulsions ceased at the operation, but on the tenth day the patient suddenly became cyanosed and died. Autopsy gave no information as to the cause of death; there were no signs of infection, but there was a large quantity of serous fluid throughout the peritoneal cavity. His second case was thirty-nine years of age, a primipara, a very large woman, having a blood-pressure of 160 systolic. Internal examination showed a very long, firm, conical cervix, with no dilatation. The patient had four severe convulsions in the two hours following admission. At section the abdominal wall was very thick and boggy and there was a large quantity of fluid in the peritoneal cavity. The operation proceeded without special difficulty, but on the following morning the patient had a convulsion and also one in the evening. She steadily improved, and six days after operation the urine showed a very faint trace of albumin. The abdominal wall broke down and the wound did not unite; under anesthesia the edges of the wound were freshened by rubbing with a hot abdominal pack and silkworm-gut sutures were introduced, and ultimately she made a good recovery, with an excellent abdominal scar.

Cesarean Section in Twin Pregnancy, with Unusual Complication.—CONWAY (*Am. Jour. Obst.*, June, 1918) reports the case of a primipara, aged forty-one and a half years, who had good general health, but during the last two months of pregnancy suffered considerable pain over the whole abdomen and marked constipation, with loss of appetite. For a week prior to admission to the hospital she was ill with peritonitis. On examination there was slight albuminuria and a positive Wassermann reaction. Pelvic measurements were practically normal. Pain had begun twenty-four hours before admission, and had lasted forty-eight hours, with but little progress. An attempt was then made to dilate and deliver by forceps under an anesthetic, but the cervix could not be dilated. After the patient had had irregular uterine contractions without progress for three days she was operated upon by section. On opening the abdomen the uterus was very large and adherent to the peritoneum, a child, weighing $6\frac{1}{4}$ pounds, and a placenta, adherent and thrombosed in many places, were delivered; a second child was rapidly delivered, with a normal placenta. Although the first child was asphyxiated at birth it was revived. The appendix was postcecal and embedded in an inflammatory mass. There was no gangrene and no free pus, but unquestionably the peritonitis originated in the appendix. The patient was stimulated freely and reacted slowly. Her convalescence was complicated by chills and excessive sweats and bad action of the heart. Pus formed and gravitated to the cul-de-sac, when it was easily removed by vaginal puncture and drainage. The patient then improved rapidly and mother and two children left the hospital in good condition.

Spontaneous Evolution of a Transverse Presentation.—MOUNT (*Am. Jour. Obst.*, June, 1918) reports the case of a negro multipara who in previous labors had escaped complications. There had been slight pain for two days, which increased considerably, and the doctor in attendance had diagnosed breech presentation. Very hard pain developed during the second stage, bleeding became less and the placenta was not felt; the cord prolapsed and ceased to pulsate. The fetal heart could not be heard at any time. The presenting part by vaginal examination could not be identified. In the midst of a hard pain the patient spontaneously expelled the child and placenta. The child was stillborn, slightly macerated and weighed 3 pounds 15 ounces. When the child appeared it was apparently in transverse position, shoulder presentation. These cases are possible only when the pelvis is of ample size, the patient a multipara and expulsive pains exceedingly strong.

Mortality among Women from Causes Incidental to Childbearing.—DUBLIN (*Am. Jour. Obst.*, July, 1918) contributes a paper upon this subject, based upon his experience in the Metropolitan Life Insurance Company of New York. The time was a period of six years, 1911 to 1916, and 14,694,260 women had been insured. These were between the age of fifteen and forty-four years, and included negro women as well as white, living in nearly all the States of the Union and Provinces of Canada. Most of these were women who worked, many of them foreign-born, among whom the birth-rate is usually somewhat higher

than among the native population. These women had, however, a well-organized visiting nurse service who cared for them during and after confinement. This material was valuable for study because the statistics were carefully made. The women were those greatly influenced by economical conditions, and one could trace among them the beneficial effect of the trained nursing service. In studying this problem the specific death-rates were limited to females of childbearing ages, fifteen to forty-four years. The statistics were made up for five- and ten-year periods, and the death-rates are thus based on death and life-rates homogeneous, with respect to sex and age. In 10,056 deaths from disease and conditions incidental to childbirth were found between the age of fifteen and forty-four years, and these occurred in the six-year-period. This gives a death-rate of 68.4 for each 100,000 women. Of these deaths, 8288 occurred among white women and 1768 among colored, the rate per 100,000 being 66.1 for the whites and 82.3 for negroes. Among these 10,056 deaths were 4321 from septicemia; 43 per cent. of the total deaths, next in importance, was albuminuria and convulsions, 2654 deaths or 26.4 per cent. of the whole. These two conditions accounted for 69.4 per cent. of the puerperal cases, but the actual proportion is even higher; this arises from the fact that many of these cases are not accurately reported. On examination the mortality rate of the white and negro races it is found that the mortality-rate from septicemia in the whites is 27.9 and in the negroes 38.5 for 100,000. The mortality-rate for puerperal hemorrhage is slightly lower for negro women, and this is true of other puerperal diseases and conditions. When the question of age is considered the least deaths occur from all diseases and conditions incidental to childbirth among white women between fifteen and nineteen years, namely, 24.3 in 100,000; this rate rises rapidly to 93 between twenty-five and thirty-four years and then falls to 62.2 from thirty-five to forty-four years. Among negroes between the age of fifteen and nineteen years the rate is 93.4 for 100,000, the same practically as that among the whites of twenty-five and thirty-four years. In general, while among the negro the maternal mortality is four times that of the whites between fifteen and nineteen years and more than one-quarter greater between twenty and twenty-four years, for the age after twenty-five and up to forty-four years the mortality-rates of negro females from puerperal conditions are lower than the rates for the whites. As regards puerperal septicemia its highest mortality is between twenty-five and thirty-four years and its lowest rate between fifteen and nineteen years among white women; among negroes there is a high rate between fifteen and twenty-four years, with very little decline between twenty-five and thirty-four years; from thirty-five to forty-four years the rates for whites and negro women are practically the same. Albuminuria and convulsions are least fatal among white women between fifteen and nineteen years and the maximum of 22.6 between the age of twenty and thirty-four years. Negroes show a maximum rate between fifteen and nineteen years of 36.9 for 100,000, with a gradual decline to forty-four years to 13. In the accidents of pregnancy a very large proportion of the fatal cases are due to attempts at abortion. Among white women the death-rate from all accidents in pregnancy is comparatively low until twenty-five years is reached; the highest rate 8.7 per 100,000 is found between the age of twenty-five and thirty-four

years. Negro women have a higher accident rate than white, especially under the age of twenty-five years; between twenty and twenty-four years the negro death-rate is 10.3, or more than twice that of the whites. Puerperal hemorrhage includes placenta previa and retained membranes provided there is no question of septic infection. The mortality-rate is least in the youngest ages among the whites and reaches the highest between twenty-five and thirty-four years, 8.1 per 1000. Among negroes it is highest between twenty-five and thirty-four years. Negro women suffer from puerperal hemorrhage much less frequently than the whites. So far as the mortality-rate in parturition is concerned, in the accidents of labor between fifteen and nineteen years among negroes the rate is five times that of the whites. Among white women most fatal accidents occur between the age of twenty-five and thirty-four years, 1.4 per 100,000, while among negroes it is earlier. It is significant to know that at the present time there is one maternal death in every 100 to 200 cases of pregnancy and childbirth; this, however, is a result obtained by studying large centers of population and the risk of maternity is second to only that of pulmonary tuberculosis; the importance of prenatal work therefore becomes evident. The value of conservation is seen in the fact that in 1916 nurses employed in caring for maternity cases made 243,738 visits. Study of statistics show definitely a very marked lessening in maternal mortality and morbidity following the work of the visiting nurses.

Cesarean Section for Contracted Pelvis, Double Uterus and Multiple Fibroids.—YOUNG (*Am. Jour. Obst.*, July, 1918) reports the case of a patient, aged twenty-eight years, six months pregnant. On examination two vaginas were found and both cervixes. Abdominal examination showed a six months' pregnancy, with marked enlargement on the right side. The pelvic measurements indicated a markedly contracted pelvis, and the symphysis was distinctly bent. An elective operation was chosen and the patient kept under observation. In the eighth month the patient went into labor and a foot protruded from the vagina; the fetal heart sounds were not heard. The patient was at once subjected to operation, when the two uteri were found blended, with small fibroids in the right fundus; there were two tubes and two ovaries. Uterine incision was made vertically as near the middle line as possible from the right uterus a female child was delivered alive. The mass which had been mistaken for the fetal head was found to be a pedunculated fibroid attached to the lower portion of the posterior wall of the uterus. Supravaginal hysterectomy was performed, leaving the left ovary. The patient's recovery was complicated by infection of the lower third of the wound and by a lobar pneumonia, from which she recovered after severe illness. She finally did well and the incision healed completely; the septum between the two vaginas disappeared; there was a ridge on the anterior and posterior wall of the vagina showing where the septum had been; both cervixes were still present.

Nitrous Oxide Oxygen Analgesia in Normal Labor and Obstetric Operations.—DANFORTH (*Jour. Am. Med. Assn.*, July 6, 1918) has observed 663 cases, and he finds that in relieving the pain of labor it is important to administer the gas before uterine contractions become

apparent to the patient. The patient breathes in the gas three or four times, occasionally six to ten depending on the relief afforded. It is occasionally necessary to give the gas throughout the entire duration of a pain. During the second stage the obstetrician must inform the person giving the anesthetic as soon as the pain begins, so that the gas may be begun soon enough. Gas alone is only of advantage when a few breaths are sufficient; if this is not the case, 5 to 15 per cent. of oxygen should be added. While the child is in the uterus rebreathing is not used. The operator must avoid cyanosis and the patient should not be completely anesthetized, because it is desirable to retain her cooperation. During the final pain of delivery it is well to add ether, which gives, as a rule, no unpleasant effects. Ether will secure the needed relaxation, and if obstetrical operation is to be performed its use is urged. In 93 per cent. of the cases recorded, analgesia by nitrous oxide oxygen has been satisfactory. For the minor operations of obstetrics, such as repair of the perineum, episiotomy and other such manipulations, gas oxygen is an excellent agent provided it be given by skilled anesthetists.

Problems of Social Order in the Interest of Mother and Child.—The *Arch. mensuelles d'obst. et de gynéc.* contains a series of articles upon the needs for caring for the pregnant and nursing women who are working for the country, preventing criminal operations and an account of the midwife service now prevailing in France. The first article, that of protecting pregnant and nursing women working in industries, contains an account of various hygienic methods, including the limitation of the hours of work and diagrams showing rooms adapted for nursing mothers, and brings out forcibly the fact that nursing a child must not be made to a woman engaged in work a burden of fatigue, nor must it be a cause for the loss of money. A nursing mother must reduce the amount of work which she is doing, and as this will lessen her wage it is the duty of the State to make this good by some form of indemnity. This can only be brought about by the appointment of an agent or patron who will assume the supervision of each group of nursing mothers. Those who have undertaken this study await with great interest the results of the entrance of the United States into the war as to whether this will reduce somewhat the strain upon the foreign nations. In comparing the years of the war it is found that stillborn infants in the year preceding the war were 7.69 for 100; in the first year of the war 6.63 for 100 and in the second year of the war 7.67 for 100. In the year before the war 3 children in each 100 were sent away from Paris to be cared for; during the first year of the war this rose to 13.35 for each 100 and during the second year to 22.32 for each 100. In the year before the war 4.98 infants were abandoned by their mothers; this number fell during the first year to 2.88 for each 100 and during the second year 5.25 for each 100. The result of the war is shown in the condition of children born before the war and during the war; thus in the year preceding the war in 100 cases 33.43 were brought to full term, while during the first year of the war 56.40 were brought to term and during the second year of the war 54.76. It is surprising to note that there has been an actual lessening in premature births since the war began; thus in the year preceding the outbreak the percentage of premature births was 66.7, which dropped

to 43.60 in the first year of the war and to 45.25 in the second. During the first two years of the war newborn children weighed distinctly more than in the year preceding the outbreak of the conflict and the number of children deficient in weight diminished during the first two years. So the mortality from puerperal diseases dropped from 0.67 for 100 to 0.46 in the first year of the war and 0.48 in the second. Several explanations may be given for this condition of affairs, one that mothers received more care than previously and another that a feeling of patriotism induced them to care for themselves and their offspring. Different European countries have different laws concerning the employment of pregnant and nursing women in various forms of industry, and in each case these laws must be made to meet local conditions. In France it has been proposed to give to each mother nursing an infant 20 francs a month as an aid in her support. Scarcely less important than the care of pregnant and nursing mothers is the prevention of criminal abortion. This may be done in several ways: by the establishment of secret or confidential maternity centers which will care for all pregnant women without asking their identity; by special hospital wards for pregnant patients where women at all stages of pregnancy can receive admission; by police regulations against the production of abortion and employment of means to prevent conception and by the aid of the medical profession in the exercise of their influence in this important matter. The situation of the midwife in France also receives attention and maps are produced showing the relative number in different portions of the country and certain reforms are outlined to increase the efficiency and standing of midwives. For this purpose it is necessary to limit the number authorized to exercise the rights of their profession and to redistrict the country with reference to the number of births occurring in each locality. It is also essential to exercise a proper supervision over infants in nursing-homes or wet-nurses and to consult with wet-nurses and those having homes for infants. The midwife must be assured an honorable life by the payment of sufficient indemnity to enable her to live decently and lay aside something for old age. Every five years midwives should serve in an obstetric clinic or a maternity hospital having a medical faculty for at least fifteen days in order to prove their ability and to learn whatever advances in obstetrics may have been discovered. Furthermore, the professional obligation of midwives should be very clearly defined and also their rights in the matter of compensation and the conditions under which they are to live in private houses.

Tetanus Neonatorum.—ROBLES (*Nederl. Tijdschr. v. Geneeskunde*, Amsterdam) reports 3 severe cases of tetanus neonatorum, of whom 1 died and 2 recovered. He used narcotics, such as chloral, ether, chloroform and morphin freely. These substances seemed to have a direct action in the toxins produced in tetanus as well as their quieting effect upon the nervous system. It was also useful to put these infants in incubators in a dark room, as this protected them against disturbance and irritation of every kind. The infants were nine, thirteen and fifteen days old, and on several occasions 120 units of antitetanus serum was injected. The incubation period seemed to be eight, ten and eleven days. Recovery from tetanus in newborn infants is exceedingly rare.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL,
BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE
WASHINGTON, D. C.

Bacteria of Gangrenous Wounds.—MAJOR H. R. DEAN and CAPTAIN T. B. MOUAT (*British Med. Jour.*) report that the cases which provided material for this investigation were selected from those undergoing treatment at the third Northern Hospital, Sheffield. In nearly all there was evidence of the presence of necrotic or gangrenous tissue in the wound, but few presented the clinical features of emphysematous gangrene. From fragments of necrotic tissue or of the discharges from the deeper parts of the wound, smears were made on blood-agar and, in some cases, on MacConkey's medium to identify aerobic organisms. To isolate and identify anaerobic organisms a tube containing about 5 c.c. of broth was heavily inoculated with the material to be examined. An egg broth was employed in several instances in place of the regular broth. Glucose agar was found to be most suitable for anaerobic plate cultures. Cultures were also made on Dorsett's egg medium. The following table shows the results of 18 cases under observation.

No. of cases.	Gas observed in tissues.	Symptoms of tetanus.	Fatal.	<i>B. edematis maligni.</i>	<i>B. aërogenes capsulatus.</i>	<i>B. tetanus</i>
1	0	+	0	+	+	0
2	+	0	+	+	+	0
3	0	0	0	+	+	0
4	0	0	0	0	0	0
5	0	0	0	+	0	0
6	0	+	0	+	0	+
7	0	0	0	+	0	0
8	0	0	0	+	+	0
9	0	0	0	+	+	0
10	0	0	0	+	+	+
11	0	0	0	+	+	0
12	0	0	0	+	+	0
13	0	0	0	+	+	0
14	+	0	0	+	+	+
15	0	+	0	+	+	0
16	0	+	+	0	+	+
17	+	0	+	+	0	0
18	+	0	0	+	+	0

Streptococci were isolated from nearly all the cases and seemed to be of one type. Staphylococci were isolated less frequently than might have been expected and, when present, they were usually not

numerous. *B. coli* was isolated from 4 cases and a proteus bacillus from Case No. 5. Of the three anaërobic bacteria present, *B. aërogenes capsulatus* and *B. edematis maligni* differ greatly in shape and in staining reaction under different cultural conditions and therefore, the identification from a smear alone may be difficult. The nature of the culture medium and the age of the culture affect the results of the Gram method of staining and also the formation of spores. The different varieties showed different rates of growth. After two or three days' incubation the broth may appear to contain a pure culture of *B. aërogenes capsulatus* and after further incubation, *B. edematis maligni* is often the predominant organism. Tetanus bacilli may not appear until after ten days' incubation. The cultural characteristics of the various strains were examined on agar, glucose agar, broth, litmus milk and Dorsett's egg medium and the reactions produced with various sugars and alcohols were recorded. A pure culture of *B. edematis maligni* was isolated in 15 cases, all of which were cases in which considerable laceration and necrosis of tissue had occurred. Only 3 of these cases were fatal, and of these, 1 showed a large gas-containing abscess, 1 was a case of tetanus, and the other showed complications. There is, therefore, no reason apparently to think that the presence of this microörganism in a wound is of serious import. The cultures isolated showed typical staining and cultural characteristics. *B. aërogenes capsulatus* was isolated from 13 of the 18 cases, but of these only 2 were fatal, death in this instance being due to tetanus. The morphology, staining and cultural characteristics of this bacillus were all typical. By a series of animal inoculations with *B. aërogenes capsulatus* and *B. edematis* it was shown that these organisms are not necessarily associated with the development of gas in tissues. They are essentially saprophytic, growing rapidly in dead tissue and producing poisons which invade the adjacent living tissue and render it a suitable medium for their growth by destroying it. The examination of films from the discharge from the wounds in the six cases, Nos. 1, 6, 10, 14, 15 and 16 of tetanus, showed no bacteriological forms resembling tetanus, but in the films made from mixed broth cultures, tetanus forms were observed in 5 cases, but only after long incubation periods. In Cases 6, 10, 14 and 16 the presence of tetanus was determined by animal inoculation with the original broth culture, and in one of these cases a pure culture of tetanus was isolated. The cultural characteristics were tested and found typical. Out of 11 guinea-pigs and 2 rabbits, which were inoculated from a ten-day-old broth culture of this strain, only 4 of the pigs succumbed. *B. tetani* were found in the discharge from the wounds of 2 patients who did not develop signs of tetanus and who had received prophylactic injections of antitetanus serum. The other 4 patients who showed signs of tetanus had had no antitoxin. The presence of *B. tetanus* is difficult to demonstrate bacteriologically and the patient may develop tetanus before a diagnosis has been pronounced. The presence of *B. aërogenes capsulatus* or *B. edematis maligni* might be taken as an indication for one or more prophylactic injections of antitoxin, which should also be injected before any operation on a patient with a gangrenous wound.

Combined Preventive Inoculation against Typhoid and Paratyphoid Fever and Bacillary Dysentery.—J. PRATT JOHNSON and A. J. MILNE (*British Med. Jour.*, January 15, 1916) state that the use of mixed bacterial vaccines has been shown to have a sound experimental and clinical basis, and great success has followed their use. The authors have investigated the possibility of combined preventive inoculation against typhoid and paratyphoid with that against dysentery. The great toxicity of B. dysentery offered a serious difficulty in the use of dysentery vaccine. This was overcome by employing the method of Broughton-Alcock (*British Med. Jour.*, August 8, 1914), which consisted of the use of a dysentery vaccine completely sensitized with a heated polyvalent dysentery serum. The vaccine prepared contains the Shiga, Flexner, Krause, Hiss and Russell strains in equal proportions, and 50 inoculations were carried out. A few inoculations were conducted with varying doses of untreated dysentery vaccine. Conclusions: (1) Inoculations with untreated dysentery are impossible, owing to the severity and duration of the local reaction. (2) Complete sensitization of dysentery vaccine produces marked reduction in local reaction. (3) The use of a typhoid and paratyphoid vaccine combined with sensitized dysentery vaccine can be employed in doses sufficiently large to produce a satisfactory immunity while the local reaction is, in all cases, slight. Such a vaccine should contain 1 c.c. of B. typhosus, B. paratyphosus A and B, 500,000,000 in a ratio of 2, 1, 1 plus B dysentery (sensitized), 250,000,000. A dose of 1 c.c. is recommended as a first inoculation followed by a second inoculation of the same amount after seven or eight days. The injections should be made in subcutaneous tissue over muscle. (4) After one inoculation of a combined untreated vaccine, specific agglutinins are found in the blood after an interval of nine to fourteen days for each of the organisms present. Immunity, therefore, is rapidly produced.

Methods of Destroying Lice.—In view of the fact that typhus fever is conveyed by the louse the control of this insect is a matter of public health importance. KINNOCH (*British Med. Jour.*, 1915) found that heat is more effective than moist heat in destroying lice and other insects. The louse can be revived after immersion for one minute in other insects. The louse can be revived after immersion for one minute in water at 100° C. Exposure to dry heat at the same temperature, and for the same time, appears to kill both lice and nits. The paraffin bodies are actively insecticidal, and of these gasoline is the most effective. Lice and their eggs are destroyed by immersion in gasoline for one minute and they may be killed by exposure to the vapor of gasoline for half an hour. Powerful fatty solvents, such as benzene, toluene and acetone, are just as toxic to lice as gasoline. Certain chlorin derivatives of methane, ethane and ethylene are more lethal to lice than any other substances and have the important merit of being non-inflammable. Immersion in the chlorin derivatives of ethane and ethylene immediately destroys all lice and nits and exposure to the vapor of these substances for five minutes is equally destructive. Even soap solutions containing 2 per cent. of trichlorethylene or 10 per cent. of tetrachlorethane are capable of killing in half an hour at the ordinary

temperatures all lice and nits. A 25 per cent. solution of dichloroethylene or trichloroethylene in vaseline when applied to the human body has been found capable of exerting its insecticidal action for hours. A 25 per cent. solution of gasoline in vaseline is of shorter duration, but is effective for some hours. The common phenol disinfectants fail to kill lice or nits at ordinary temperature. The volatile oils have no direct insecticidal effect. The human body anointed with sulphur, balsam of Peru, mercury ointment and hellebore ointment do not prevent the hungry louse from feeding. For practical purposes it has been found that the destruction of lice and nits is best secured by immersion of garments and body clothes in a gasoline or benzine bath. Danger from fire and waste of gasoline are avoided by using such a bath and extractor as are employed in a dry-cleaning apparatus. For personal prophylaxis it seems certain that lice would not continue on the human body if anointed daily with a 25 per cent. solution of trichloroethylene in vaseline or on the body anointed twice daily with a solution of gasoline in vaseline of similar strength.

Production of Antipneumococcus Serum.—COLE and MOORE (*Jour. Exp. Med.*, October 1, 1917) state that in the production of immune serum for therapeutic purposes strict attention must be paid to the immunological specificity of the bacteria used for immunization. At present the only serum of which the therapeutic value has been proved is that effective against Type I pneumococcus infection. This serum should have agglutinating power for Type I pneumococcus and should have the power of protecting mice against large amounts of virulent culture. Experiments have shown that for producing the primary immunity most rapidly several series of small doses of dead cultures should be given, the injections being made daily for six or seven days, followed by a week in which no injections are made. To produce the highest type of immunity probably living organisms are required. These should be given in moderate doses daily for three days with an interval of a week between each series of injections. By following accurately the methods described, horses may be made to produce rapidly a high grade of specific serum. The observations so far made indicate the importance of employing small doses of culture frequently repeated in this form of immunization.

Suggestions Concerning the Prevention and Cure of Acute Lobar Pneumonia.—COLE (*Am. Jour. Pub. Health*, June, 1917, vii, No. 6) reports briefly some of the late observations and conceptions concerning prevention and cure of acute lobar pneumonia and includes a résumé of some work done at the hospital of the Rockefeller Institute. He emphasizes the fact that over half the cases of acute lobar pneumonia occur between the ages of twenty and fifty years, the period of greatest activity. Many laymen and physicians are prone to regard pneumonia as a disease of the very young and the aged. About 65 per cent. of the cases of acute lobar pneumonia are caused by pneumococci of Types I and II, types which are immunologically quite distinct and have definite, specific characters. The mortality rate among cases infected by these organisms is 25 to 35 per cent. A third type of organism

causes pneumonia in only about 10 per cent. of the cases. Most of the pneumococci found in mouths during health belong to Type IV. Of 942 normal individuals studied in the hospital of the Rockefeller Institute, 450 or 47 per cent., were found to harbor pneumococci, and group IV claimed 345 out of the total. Types I and II appeared in 56 instances. In all but 3 of the cases in which Types I or II were isolated from normal individuals the healthy individuals had been in close association with a person sick of pneumonia caused by the same type of pneumococcus. In studying the length of time convalescents or healthy carriers might harbor organisms belonging to Types I or II it was found that in most cases the organisms belonging to these types die out in the mouths of convalescents within a few weeks. The longest time in which any organisms have been observed in the mouth of a convalescent has been eighty-three days. The same facts hold good concerning the persistence of Types I and II in the mouths of healthy carriers. Study of dust in houses where pneumonia was present and in houses where no known cases of pneumonia had occurred showed the following interesting results: From 175 specimens of dust from houses which had contained pneumonia due to Type I or II, 73 specimens showed pneumococci, and of this number 47 belonged to Types I or II. In only 2 cases did the type of pneumococcus found in the dust fail to correspond with the type isolated from the patient. Sixty-two specimens of dust from houses where no cases of pneumonia were known to have existed were studied. Of these specimens 18 showed pneumococcus and only 1 was of Type I or II and in this case the known carrier of the corresponding fixed type was found to be visiting at the time. Infections from Type III, which causes the most severe pneumonia, are somewhat baffling in the effort to discover their source. In an examination of 450 healthy carriers, group III appeared 85 times, and in practically none of these persons could any association with cases of pneumonia due to the same type of organism be discovered. It has been proved that these healthy carriers may harbor group III organisms even for years, and as yet no difference of any character has been found between the Type III organisms found in disease and those found in the mouths of healthy carriers. With reference to preventive inoculation the author appears to think that among troops preventive inoculation might be tried with considerable hope of success, although the results of its use in civil population hitherto have been disappointing. The author recommends in conclusion: (1) That pneumonia be made a reportable disease; (2) that patients be isolated, sputum sterilized and that the rooms occupied by pneumonia patients be thoroughly cleansed at least with soap and water (if not disinfected); (3) that for statistical purposes health departments should determine the type of pneumococci in pneumonia cases; and (4) that utmost speed be exercised in identification of the type of pneumococcus in a given case when it is intended to employ serum treatment, the greatest benefit being obtained by the earliest possible administration of the serum in appropriate cases.

Bacteriology of the Bubble Fountain.—PETTIGONE, BOGART and CLARK (*Jour. Bact.*, 1916, No. 5, i) reported the results of an investigation made as the result of an epidemic of streptococcus tonsillitis in

which the bubble fountains were suspected to be a factor in transmitting disease. A survey of all the fountains of the University of Wisconsin showed the presence of streptococci in over 50 per cent. of the total number. The streptococci varied in abundance from a few chains to an almost pure culture obtained by swabbings from the fountains in the woman's dormitory. In an experimental bubble fountain, *Bacillus prodigiosus*, when introduced either by means of a pipette or by the moistened lips, remained in the water from 2 to 135 minutes, depending partly on the height of the bubble. Most of the organisms are flushed away, but some remain, dancing in the column much as a ball dances on the garden fountain, even though the bubble be increased to the impractical height of four inches. To avoid the difficulty always present in the vertical column a simple fountain with a tube at an angle of 50 degrees from the vertical was constructed. *Bacillus prodigiosus* was never found in the plates from this type of fountain even when samples were taken immediately after the introduction of the organism. It is believed that this type of fountain should be generally adopted. Its simplicity, low cost of construction and freedom from lurking danger should recommend it to all.

Effects of Exposure to Cold upon Experimental Infection of the Respiratory Tract.—MILLER and NOBLE (*Jour. Exper. Med.*, 1916, No. 3, xxiv) state that respiratory infection of rabbits with *Bacillus bovisepcticus* (snuffles) is favored by chilling the animals after they have been accustomed to heat. The character of this disease, which occurs frequently in rabbits under natural conditions, make the application of the experimental results to similar respiratory conditions in man less open to objection than in similar experiments with other infections. The weight of experimental evidence, including that of the authors, does not justify the elimination of exposure to cold as a possible secondary factor in the incidence of acute respiratory disease. From the limited data of their last two experiments, they suggest that any marked change of temperature predisposes rabbits to this infection, the severity of which varies with the amount of change, and that a change from low to high temperature has even more effect than that from high to low.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this JOURNAL.*

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

INDEX.

A

- ABDOMINAL cases, selection of, for operation, 606
viscera, wounds of, 147
Abortion in absence of uterine pregnancy, 291
Acid excretion in pneumonia, 619
Acidosis in pneumonia, 619
Acriflavine, 750
Adrenal gland, focal necrosis of, 313
Air raid case, 457
Albuminuria, 643
Alkali reserve in blood of pellagrins, 442
Allen, W., typhoid vaccine in typhoid spine, 11
Ambrine, 753
American Journal of Care for Cripples, 113
Analgesia, 905
Anemia, aplastic, 799
Anesthesia in labor, 139
Anoci-association, application of, to obstetrics, 139
Anopheles infectivity experiments, 623
punctipennis, 779
Antigen dose and antibody production, 460
precipitin, 618
Antipneumococcus bodies, 773
serum, 461, 911
Antiseptics on toxin of *Bacillus welchii*, 616
Antisheep hemolytic amboceptor in glycerol, 462
Apfelbach, G. L., early diagnosis of lead poisoning, 781
Appendicitis, chronic, 494
carcinoma of, 190
Arsphenamin injections, nitrotoxic crises after, 758
Arteries, coronary, anatomy of, 706
Arthritis, chronic, 702
teeth and tonsils as factors in, 541
treatment of, 757
Arthroplasty, new joint formation in, 603
with aid of animal membrane, 604
Asthma, bronchial, 747
Asthmatoid wheeze, 625

- Atropin test in typhoid fever, 288
Auricular hypertrophy, 17

B

- BACILLARY dysentery, 910
Bacilli, hemophilic, 463
tubercle, in urine, 636, 775
Bacteria of gangrenous wounds, 908
Bacteriology, intestinal, 157
of the bubble fountain, 912
Bárány tests as applied to aviators, 146
Barley as a food material, 432
Barron, M., meningitis in the newborn and in early infancy, 358
Beck, H. G., fat redistribution in the hypophyseal type of dystrophy adiposogenitalis, 711
Bell, R. D., open pneumothorax, 839
Bile peritonitis, 603
Bile-soluble diplococci, 148
Black, D. R., hemangioma of liver, 469
Blood cells, transfusion with, 896
counts in non-infective surgical conditions, 287
plasma and kidneys, 1
pressure in albuminuria, 643
in cardiac dilatation, 749
in head traumas, 287
in hemorrhage, 749
in pregnancy, 608
in shock, 749
transfusion, 606, 609, 748
Blum, S., focal infections in childhood, 681
Bock, A. V., electrocardiographic evidence of abnormal ventricular preponderance and of auricular hypertrophy, 17
Boggs, R. H., comparative value of radium and roentgen radiation, 690
Bone, regeneration of, 752
Bovaird, D., irritable heart or effort syndrome, 872
Bradbury, S., influenza epidemic in soldiers, 737
Bronchial asthma, 747
Brooks, H., hyperthyroidism in the recruits, 726

- Bruck precipitin test for syphilis, 134
Bubble fountain, 912
- C
- CAMAC, C. N. B., lobar pneumonia treated with antipneumococcus serum, 887
Canned goods, 310
Carcinochondrosarcoma of the mouse, 769
Carcinoma of cervix, 128
 pathogenesis of, 619
 of pregnant uterus, 607, 767
 of vermiform appendix, 190
Cardiac dilatation, 749
Carrel-Dakin treatment, 118
Casualty clearing station, 258
Cerebral tumor, 294
Cerebrospinal fever, 132, 270
 meningitis, 133
Cervix, bloodless repair of, 768
Cesarean section for contracted pelvis, 608, 905
 for double uterus, 905
 for eclampsia, 902
 for multiple fibroids, 905
 through lower uterine segment, 766
 in twin pregnancy, 903
Chalazion, 143
Cheney, W. F., diagnosis of chronic appendicitis, 494
Chenopodium, oil of, 131, 754
Chest, pleural infection in wounds of, 895
 war surgery of, 285
 wounds of, 286
Chick embryo, tumors in, 770
Chicken-pox, 459
Childbearing, mortality in, 903
Childhood, focal infections in, 681
Cholelithiasis, 239
 studies in, 564
Cholera carriers, 153
 hog, 464
 immunization, 154
Cholesterohydrothorax, 20
Choroid plexus, 468
Clendenning, L., reinfection with streptococcus hemolyticus in lobar pneumonia, measles and scarlet fever, 575
Cold, effects of exposure to, 913
Colds as a possible source of contagion for pneumonia, 289
 common, 780
Collins, J., clinical display of syphilis of the nervous system, 375
Common colds, 780
Communicable diseases in schools, 152
Complement-fixation in Hodgkin's disease, 720
- Corn and wheat, properties of foods derived from, 309
Crohn, B. B., estimation of stomach contents, 656
Curette in cases of infection, 447
Cyanocuprol, Koga's, 78
Cystocele operations, 451
- D
- DAVENPORT, C. B., multiple neurofibromatosis, 507
Delinquents, physical condition of, 308
Derby, G. S., effects of mustard gas on the eyes, 733
Dermatitis venenata, 458
Dermatology in connection with the war, 119
Diabetes mellitus, 747
Dichloramine-T in wounds, 748
Diphtheria antitoxin in blood sera, 152
 carriers, 774
Diplopia, 454
Dogs, senescence in, 311
Drainage tubes, abuse of, 897
Drinking fountains, 778
Duodenal contents, examination of, 817
Duty, performance of, by military officers, 780
Dysentery, 453
 bacillary, 910
Dysmenorrhoea, 769
Dystrophy adiposogenitalis, 711
- E
- EAR, concussion injury of, 614
 diseases of, in Egypt, 611
 injuries to, from high explosives, 144
 radium in diseases of, 146
 war injuries of, 302
Eclampsia, 293
 Cesarean section for, 902
 postpartum, 294, 610
 without convulsions, 295
Ectopic contractions, 557
Eczema due to deficient thyroid secretion, 460
Einhorn, M., examination of the duodenal contents, 817
Electrocardiogram, ventricular deviation in, 894
Empyema in base hospitals, 899
Enteric fever, 623
Enterocolitis, 173
Enterostomy for ileus, 128
Epithelioma of the skin, 148

- Erickson, R. J., blood-pressure and kidney function findings in orthostatic albuminuria, 643
- Ethyl chloride as an anesthetic, 285
- Evolution, spontaneous, 903
- Exophthalmic goitre, 369
- Eye diseases, tuberculin in, 453
- Eyeball, tension of, 452
- Eyes, artificial, disinfection of, 454
- F
- FACE presentation, 136
- Factors in relations between blood plasma and kidneys, 1
- Flavine, treatment of wounds by, 432
- Focal infection, 248, 613
- Food for children, 431
- Fountains, bubble, 912
drinking, 778
- Frazier, C. H., operable tumor involving the Gasserian ganglion, 483
- G
- GALVANIC method of testing function of inner ear, 456
- Gangrene, gas, 614
- Gangrenous wounds, bacteria of, 908
- Gas-bacillus infection in France, 129
- Gas gangrene, 614
- Gasserian ganglion, tumor of, 483
- Gastric juice, 151
hypomotility, 795
- Gellhorn, G., vaginal metastases of hypernephroma, 94
- Gibson, C. L., surgical treatment of war wounds, 253
- Glands, salivary, tumors of, 896
- Glossodynia, 248
- Glycerol, 462
- Goitre, 248
exophthalmic, 553
- Graham, E. A., open pneumothorax, 839
- Granuloma inguinale, 147
- Guillotine amputation, 286
- Gunshot wounds and their treatment, 441
of knee-joint, 439
of lungs, 440
of pleura, 440
treatment of, 263
- Gutta-percha-paraffin substitute, 753
- H
- HAMMOND, R., teeth and tonsils as causative factors in arthritis, 541
- Head, ramrod wound of, 752
- Heart, disordered action of, 132
irritable, 872
sarcoma of, 214
- Hemangiomas of skull and bilateral cystic adrenals, 469
- Hematocolpos, 448
- Hemoglobin in hemorrhage, 749
in shock, 749
- Hemolysis in transfusion of babies, 764
- Hernia, pudendal, 394
- Heterologous tumor grafts, 771
- Hodgkin's disease, 720
- Hog cholera, 464
- Human serum and Wassermann reaction, 462
- Hydatidiform mole and chorio-epithelioma, 446
- Hypernephroma, 94
- Hyperthyroidism in the recruit, 726
- Hypomotility, gastric, 795
- I
- ILEUS, enterostomy for, 128
- Illumination for operations, 453
- Influenza epidemic in a camp, 757
of 1918, 757
pneumonia, 901
- Interstitial pregnancy, 610
- Intestinal bacteriology, 157
- Intrapericardial traumatic hemorrhage, 130
- Iodide solutions in roentgenography, 296
- Iodides of strontium, sodium and potassium, 288
- Iritis, 142
and cystitis in dysentery, 453
- Irritable heart of soldiers, 432
- J
- JACKSON, C., new diagnostic sign of foreign body in trachea or bronchi, the asthmatoïd wheeze, 625
- Janney, N. W., ochronosis, 59
- K
- KANGAROO walk in puerperal retroversion, 291
- Kelly, T. H., diaphragmatic pleurisy, 808
- Keloid treated by creosoted oil, 458
- Kendall, A. I., developments in intestinal bacteriology, 157

- Kidney function, estimation of, 830
 Kidneys and blood plasma, 1
 Knee-joint, gunshot wound of, 439
 Koga's cyanocuprol, 78
 Kristjanson, H. T., complement-fixation in Hodgkin's disease and allied affections, 720
- L**
- LABOR complicated by rupture of the vagina, 763
 induction of, for pelvic deformity, 766
 management of third stage of, 295
 obstructed by a contraction ring, 445
 rectal and vaginal examination of, 760
 Labors, emergency, 610
 Labyrinth, disease of, 613
 Late workers, 311
 Lead poisoning, 781
 Leprosy and tuberculosis, 30
 Levy, I. H., the opaque meal versus the stomach tube in gastric hypomotility, 795
 Lice, methods of destroying, 910
 Liver, hemangioma of, 469
 Lungs, gunshot wounds of, 440
 Lymphosarcoma, 463
 Lyter, J. C., autoserotherapy in tuberculous pleurisy, 665
- M**
- McCONNELL, G., meningococcal cerebrospinal meningitis, 105
 McCrudden, F. H., influence of radium water therapy on creatinin and uric acid metabolism in chronic arthritis, 702
 Macallum, A. B., factors in relations between blood plasma and kidneys, 1
 Magnesium and calcium, effect of, after lethal doses, 756
 Major, R. H., hemangioma of the liver, 469
 Malaria, 131
 Marino, F., cerebrospinal fever, 270
 Market milk, 299
 Moschcowitz, A. V., pudendal hernia, 394
 Mason, E. H., blood-pressure and kidney function findings in orthostatic albuminuria, 643
 clinical value of the estimation of kidney function, 830
 Mastitis in the cow, 466
 Mastoiditis, 455
 Masuda, T. I., clinical experience with Koga's cyanocuprol, 78
 Matsuda, T. K., clinical experience with Koga's cyanocuprol, 78
 Measles, 575
 Melanoblastomas of the eye, 301
 Mendenhall, D. R., a memorandum on milk, 586
 Meningitis, meningococcus, 745
 in the newborn and in early infancy, 358
 Meningococcus carriers, 465, 776
 meningitis, 745
 Menstruation, influence of, on acidosis in diabetes mellitus, 747
 Mercuric chloride intoxication, 755
 Mercury applied by inunction, 290
 Meyer, A. W., side-lights on multiple myeloma, 329
 Milk, a memorandum on, 586
 factors in production of, 467
 Morphine-hyoscin method of painless childbirth, 138
 Morris, M. L., meningococcal cerebrospinal meningitis, 105
 Mortality after age of forty-five years, 777
 Moschcowitz, F., focal necrosis of adrenal gland, 313
 Mosquitoes, flight of, 777
 Moving pictures, 142
 Mustard gas, 733
 Myeloma, multiple, 329
- N**
- NEPHRITIS, experimental acute, 615
 Nerves, peripheral, injuries to, 440
 Neurofibromatoses, multiple, 507
 Neuroses of otological interest, 612
 Newborn, germs in mouth and rectum of, 766
 Nitrous oxide oxygen analgesia in obstetric operations, 905
 Nose and throat, disease of, in Egypt, 611
 Nurseries, infection in, 445
 Nutrition, composition of meat under various conditions of, 431
 Nutritive value of straw treated with alkali in the dietary of man, 120
- O**
- OCHRONOSIS, 59
 Oil of chenopodium, 131
 Ophthalmia, sympathetic, 141
 Os, external, dilatation of, 759
 Osborne, O. F., suprarenal disease, 202

Osseous cyst, 751
Ovarian cyst, 135

P

PACHYPLEURITIS, 895
Paralysis and contracture, 127
Paratyphoid fever, 464, 910
Pathology of gas gangrene of muscle, 306
Pellagra, 154
 transmission of, to monkeys, 621
Percy's cold-iron method in carcinoma of the cervix, 128
Peritonitis, bile, 603
Perlstein, I., sarcoma of heart, 214
Phagocytosis under various conditions, 772
Phenol excretion in urine of newborn, 292
Pituitrin, action of, on the human uterus, 295
Placenta, previa, 138
 separation of a normally implanted, 762
Plasmodium falciparum, 779
Pleura, gunshot wounds of, 440
Pleurectomy for suppuration, 895
Pleurisy, diaphragmatic, 808
 tuberculous, 665
Pellagrins, alkali reserve in blood, of, 442
Pneumococci, 307
Pneumococcus, 773
 in sputum, 618
Pneumonia, 901
 acidosis in, 619
 epidemiology of, 774
 influenza, 901
 lobar, 575, 887, 911
Pneumothorax, open, 839
Poliomyelitis, 468, 616, 902
 epidemic, 754
 infection, 299
Postpartum hemorrhage, 292
Potter, N. B., Sahli's volume sphygmobolometer, 490
Pregnancy, twins, Cesarean section for, 903
Pregnant women, 136
Preiser, S. A., multiple neurofibromatosis, 507
Presentation, transverse, 903
Problems of social order in interest of mother and child, 906
Proflavine, 750
Prophylaxis of infection in nurseries, 445
Pruritus ani, 900
Psoriasis, 459
Pubic symphysis and forceps delivery, 294

Pudenda, granuloma of, 458
Pudendal hernia, 394
Pulse-rate in head traumas, 287
Pyoderma, 458

R

RADIUM and roentgen radiation, 690
 in diseases of the ear, 146
 in uterine cancer, 449
 hemorrhage, 449
 water therapy, 702
Rat and poliomyelitis, 902
Reckord, F. F. D., relation of housing to pulmonary tuberculosis, 670
Recruit, hyperthyroidism in, 726
Rectum, contracture of, 205
Reimann, S. P., primary carcinoma of the vermiform appendix, 190
Renal function in acute infectious diseases, 894
 tuberculosis, 289
Respiratory tract, exposure to cold upon, 913
Reviews—
 Barton, Vital Function-testing Methods, 284
 Borgey, Hygiene, 436
 Browning, Bacteriology, 437
 Cabot, Modern Urology, 434
 Dercum, Mental Diseases, 283
 Dorland, Medical Dictionary, 283
 Dumas and Carrel, Treatment of Wounds by the Carrel Method, 126
 Godlee, Lord Lister, 125
 Greenwood, Scopolamin-morphin Seminarcois during Labor, 741
 Hirst, Obstetrics, 126
 Kerley, Pediatrics, 278
 Laboratory Methods of the United States Army, 277
 Lorand, Building Human Intelligence, 281
 Lucaiani, Human Physiology, 124
 Lungs, Gonorrhoea and its Complications, 743
 McCombe and Menzies, Medical Service at the Front, 277
 McDill, Lessons from the Enemy, 276
 Manual of Splints and Appliances, 438
 Medical Record Visiting List, 283
 Nicol, Dream Psychology, 282
 Penhallow, Military Surgery, 742
 Progressive Medicine, 121
 Rose, Physical Diagnosis, 279
 Southard and Solomon, Neurosyphilis, 280
 State Board Examinations and Answers of United States and Canada, 282

Reviews—

- Surgical Clinics of Chicago, 437
 Thornton, Pocket Formulary, 124
 Vedder, Syphilis and Public Health, 741
 Wall, The Prescription, 280
 Wells, Chemical Pathology, 284
 Wheeler, Surgery, 438
 Rocky Mountain spotted fever, 150, 156
 Roemer's intracutaneous method, 152
 Roentgen plate in tuberculosis, 68
 Rothschild, M. A., cholelithiasis, 239, 404, 564

S

- SAHLI'S volume sphygmobolometer, 490
 Sarcomata, 751
 Sargent, influence of radium water therapy on creatinin and uric acid metabolism in chronic arthritis, 702
 Scarlet fever, 151, 575
 etiology of, 621
 Schneider, J. P., aplastic anemia, 799
 Seehorn, N. A., meningococcic cerebrospinal meningitis, 105
 Senescence in dogs, 311
 Serum, antipneumococcus, 887, 911
 disease, 133
 sickness, 133
 Shingles, 459
 Sigmoid colon, contracture of, 205
 Singer, J. J., relation of the physical signs to the roentgen plate in pulmonary tuberculosis, 68
 Skull, fractures of, 605
 Sluder, G. S., lingual tonsil, goitre, glossodynia and focal infection, 248
 Smith, F. M., anatomy of the coronary arteries, 706
 Smith, T. A., irritable heart or effort syndrome, 872
 Smithies, F., protozoic enterocolitis in the middle west, 173
 Sodium cyanide, 442
 iodide, intravenous injections of, 898
 Soper, H. W., magnesium sulphate solutions in spastic contractures of rectum and sigmoid colon, 205
 Sphygmobolometer, 490
 Spine, typhoid, 11
 Spirochetal flora of normal male genitalia, 312
 Spirochetosis icterohemorrhagica, 620
 Squires, J. W., typhoid vaccine in typhoid spine, 11
 Stanton, E. MacD., prognosis of exophthalmic goitre, 369
 Status lymphaticus, 40
 Sterility, 769
 Stomach contents, estimation of, 656
 emptying of, 184

- Strauss, A. E., relationship of origin of ectopic contractions to ventricular preponderance as shown by the electrocardiograph, 557
 Streptococcus and bovine mastitis, 155
 Strick, E. J., congenital absence of the uterus with anomalous vulvovaginal anus, 75
 Sugai, T., chemotherapy of leprosy and tuberculosis, 30
 Suprarenal disease, 202
 Swain, R. E., side-lights on multiple myeloma, 329
 Symblepharon, 300
 Symmers, D., status lymphaticus, 40
 Symphysectomy, 293
 Syndrome, effort, 872
 Syphilis, new pathology of, 897
 of nervous system, 375
 ocular, 141
 Wassermann test in, 749

T

- TARTAR emetic in malaria, 131
 Technic of Carrel-Dakin treatment, 118
 Tetanus neonatorum, 907
 Thymus death, 765
 Tonometer of Schiotz in practice, 301
 Tonsil infections, 461
 Tonsillectomy, 143
 Toxin-antitoxin injections, 311
 Tubal and uterine pregnancy, 140
 Tubercle bacilli from animal tuberculosis, 305
 in feces of cattle, 466
 in urine, 636
 Tuberculosis and leprosy, 30
 concepts of, 310
 in France, 415
 miliary, 618
 pulmonary, 670
 renal, 298
 Tuberculous lymph nodes, 149
 Tumor of Gasserian ganglion, 483
 Typhoid bacteremia, 618
 fever, 444, 910
 spine, 11
 vaccine, 11, 779
 Typhoid-antityphoid serum complex, 617
 Tyramin, action of, 443

U

- UPCOTT, C. H., some principles of treatment of gunshot wounds, 263
 Ureteral stricture, 296
 Uric acid metabolism, 702
 Urinary extravasations, 442

Urine, tubercle bacilli in, 636
 Uterus, absence of, 75
 prolapse of, 768

V

VACCINE, typhoid, 11, 779
 Vaginal metastases of hypernephroma,
 94
 Ventricular preponderance, 17
 Veratrum, clinical action of, 289
 Vital statistics of cities of United
 States, 310
 Vitamins, 463
 Volkmann's ischemic paralysis and con-
 tracture, 127
 Von Recklinghausen's disease, 507

W

WAR injuries, 612
 surgery, 753
 blood transfusion in, 748
 of the chest, 285
 wounds, surgical treatment of, 253

Wassermann reaction, 462, 465
 test in syphilis, 749
 Watson, E. M., methods for demon-
 strating tubercle bacilli in urine, 636
 Weems, Jr., B. F., cholesterohydro-
 thorax, 20
 Weil's disease, 620
 Weiss, H. B., diaphragmatic pleurisy,
 808
 White, F. W., effect of stimuli from the
 lower bowel on the rate of emptying
 the stomach, 184
 White, Paul D., electrocardiographic
 evidence of abnormal ventricular
 preponderance and of auricular
 hypertrophy, 17
 White, W. C., work of Bureau of
 Tuberculosis in France, 415
 Wilensky, A. O., cholelithiasis, 209, 404,
 564
 Wilson, L. B., lesions in cervical sym-
 pathetic ganglia in relation to ex-
 ophthalmic goiter, 553
 Wooler, E. W. N., reception and dis-
 tribution of cases in a casualty clear-
 ing station, 258
 Wound inspection, 311
 Wounds, gunshot, of peripheral nerves,
 898
 of the chest, 286

Elixir of Enzymes

is a palatable aid to digestion; an agreeable vehicle for iodids, bromids, salicylates, etc., and supplies the curdling ferment for making junket.

Pituitary Liquid (Armour)

(Liq. Hypophysis)

is physiologically standardized and is entirely free from chemical preservatives. $\frac{1}{4}$ cc and 1cc ampoules, 6 in box.



Extract of Red Bone Marrow

is a great reconstructive and will be found of value to patients convalescing from Influenza and other troubles.

Armour's Surgical Catgut Ligatures

are the finest thing of the kind on the market; they are strong, smooth and sterile. Plain and 10, 20, 30 and 40 day Chromic, sizes Nos. 000 to 4, inclusive. At present, 60 inch lengths only.

ARMOUR AND COMPANY
CHICAGO

An Aid in Convalescence

"Horlick's" is clean, safe and dependable. Its quality assures service and results. Fats, proteids, carbohydrates and salts are properly proportioned and in easily assimilated form to progressively build up the patient.

*This is the package
avoid imitations*

To avoid imitations

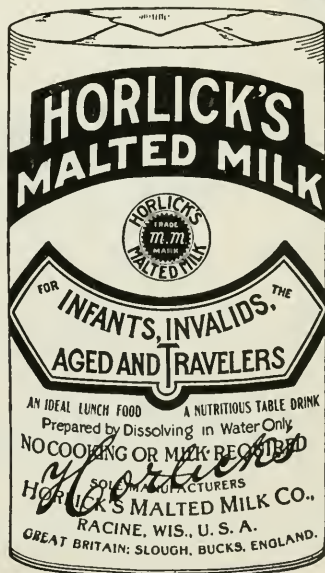
SPECIFY

"Horlick's the Original"

Samples Sent Upon Request

Horlick's Malted Milk Co.

Racine, Wis.



Chloramine-T Monsanto

An ideal antiseptic of wide applicability
Stable in powder form and in aqueous solution

FOR IMPREGNATION OF GAUZE

Practically Non-toxic
Will not coagulate blood serum
For treatment of wounds and as a general germicide

Dichloramine-T Monsanto

Very powerful antiseptic containing about 29 per cent. active Chlorine
Successfully used in

WAR and CIVIL SURGERY

5 to 10 per cent. solutions used for wound treatment
1 to 2 per cent. solutions used as spray for

NOSE and THROAT

Chlorcosane Monsanto

Most desirable solvent for Dichloramine-T

Manufactured by
MONSANTO CHEMICAL WORKS
ST. LOUIS, MO.

PNEUMONIA

MORTALITY REDUCED 25 PER CENT.

ACCORDING to Major Nichols, U. S. A., the death-rate in pneumonia has been reduced from 30 per cent. to 5 per cent. by the early intravenous administration of large doses of Antipneumococcus Serum—Type I.

The serum treatment of lobar pneumonia has passed the experimental stage and, to quote Major Nichols, "No patient with Type I infection who dies without the early intravenous administration of large doses of Type I serum can be said to have received the best treatment."

Lederle's ANTIPNEUMOCOCCUS SERUM—TYPE I standardized by animal protection tests, according to the method originally outlined by Cole, such that 1 c.c. will protect against 500,000 fatal doses of live pneumococci, Type I.

Each lot of **Lederle's** ANTIPNEUMOCOCCUS SERUM—TYPE I is safeguarded by standard tests for potency, sterility and safety prescribed by the United States Government.

Lederle's ANTIPNEUMOCOCCUS SERUM—TYPE I is marketed in special syringe packages containing 50 c.c., thus facilitating the administration of the recommended doses of 100 to 200 c.c.

Every package of **Lederle's** ANTIPNEUMOCOCCUS SERUM—TYPE I bears the date of manufacture, thus insuring the physician against the use of serum of unknown age.

Price per Bulb Syringe package of 50 c.c. \$6.50
Price per Vial package of 100 c.c., \$12.00.

LITERATURE ON REQUEST

Lederle Antitoxin Laboratories

NEW YORK

CHICAGO

KANSAS CITY

NEW ORLEANS

OTTAWA, CANADA



A HELP TO A
Better Diagnosis

See page
786

Pat. June 26, '02

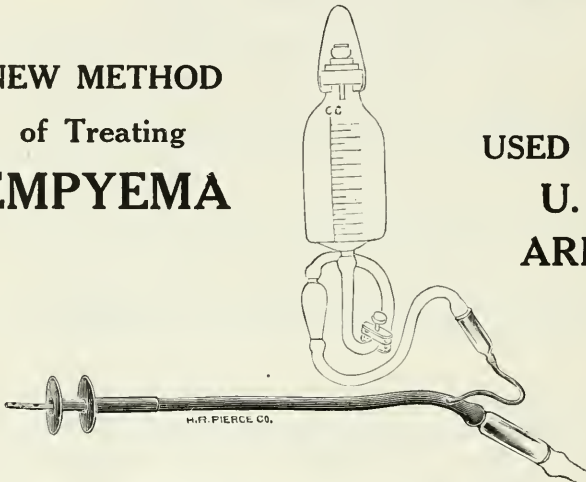
THE best authorities are agreed that the testing of blood for hemoglobin is of much importance in obtaining a correct diagnosis. You don't need an expensive hemoglobinometer. Cabot says, "The Tallquist Hemoglobin Scale makes hemoglobin estimation no more of an undertaking than feeling the pulse." White absorbent paper to take the specimen, a scale of ten standard tints for comparison, in a little book that slips into the pocket. \$1.75 postpaid. If your dealer hasn't it, order direct.

EDWARD PENNOCK, Sole American Agent
 3609 Woodland Avenue - - PHILADELPHIA

See page
786

NEW METHOD
 of Treating
EMPYEMA

USED by the
U. S.
ARMY



McHENRY-BREWER EMPYEMA TUBE

For the administration of Dakin's solution by the Carrel Method

Price of Empyema Tube	\$2.00
Price of Carrel apparatus with the heavy brown glass reservoir to prevent chemical disintegration	\$6.00

Write us for special catalogue of Newest Splints, General Operating and Bone Surgery Instruments, Carrel Instillation Apparatus, Ambrine Atomizer, Sherman Sterilization Pessary, Etc.

HARVEY R. PIERCE COMPANY

1801 CHESTNUT ST. The Modern Surgical Instrument Store **PHILADELPHIA**
 PITTSBURGH SALES OFFICE, 3030-3031-3032-3033 JENKINS ARCADE

SMALLWOOD—Biology.

*New (3d) Edition
 Thoroughly Revised*

The section dealing with the biology of cells has been entirely rearranged and extended that it may furnish a better foundation for the present-day conception of biology.

Octavo, 306 pages, 235 engravings, 8 plates. By WILLIAM M. SMALLWOOD, PH.D., Professor of Comparative Anatomy, Liberal Arts College of Syracuse University.

Cloth, \$3.00, net.

706-8-10 Sansom St.
PHILADELPHIA

LEA & FEBIGER
PUBLISHERS

2 W. 45th Street
NEW YORK

NOVOCAIN

(PROCAINE--METZ)

American Made

In the Service

We have furnished the *U.S. Government* with practically the entire output of our factory, including Novocain Powder, Novocain Tablets and Novocain Suprarenin Tablets.

This fact has restricted our output to the profession, but our increased production now enables us to supply Novocain through the regular trade channels promptly.

INSIST ON N-S TABLETS

No Harrison Narcotic Blank Required

Send Us the Name of Your Dealer

H. A. Metz Laboratories, Inc.

122 HUDSON STREET

NEW YORK

Hare's Practical Therapeutics

*New (17th) Edition
Just Ready*

The *dominating authority* on therapeutics, it places the subject of treatment before the reader so that it may be applied at the bedside in a rational manner. The revision has been most thorough.

The lessons gained from the great war as to the treatment of Shock and Collapse; the use of Ambrine and Paraffine in Burns; the latest modification of Dakin's solution; Carrel's methods; the employment of Dichloramine-T in Chlorcosane for Wounds and Burns; the treatment of Tetanus, etc., are all set forth clearly and fully. The war also has shown the need of proper methods of Intravenous Injections and of Direct Transfusion, therefore the *technique* of these procedures is given in full detail.

The article on Influenza is most timely and up-to-date, as are the sections on Vaccine and Serum Therapy. All additions and changes in the new U. S. P. are included while a comparative table shows the strength of the more important preparations in the preceding and the present Pharmacopœia. Drugs formerly made under German patents are designated by their new names—Arsphenamine for Salvarsan, Procaine for Novocaine, etc.

Part I. General Therapeutic Considerations, includes a number of important tables and covers Mode of Action of Drugs, Modes of Administering Drugs, Dosage, Absorption, Indications and Contra-indications, Classification, Incompatibility, Prescription-Writing, etc.

Part II. Lists all Drugs, alphabetically, describing them and their physiological action, therapeutics, incompatibilities, administration, preparations poisoning, contra-indications, etc.

Part III treats of Remedial Measures other than Drugs—the Antiseptics, with technique of preparing and the apparatus for using Dichloramine-T, etc.; Antitoxins; Vaccines and Serums; Electro- and Hydrotherapy; Enterocolysis; Intravenous Injection; Transfusion; Lavage; Lumbar Puncture; Phylacogens; Pollen Proteins, etc. The methods of prescribing a proper diet are described in more detail than in former editions, particularly in respect to children and diabetics.

Part IV takes up Treatment of Diseases and full definite therapeutic directions are given. Such noted authorities as Dr. G. E. deSchweinitz, Dr. Edward Martin and Dr. Barton C. Hirst revised respectively the articles on Diseases of Eye, Venereal Diseases, and Disorders of Parturition or Pregnancy.

Then follows a wonderfully thorough Therapeutic Index of Diseases and Remedies. This feature and the system of cross referencing between the part dealing with drugs and the part on diseases enable you to get any information you want in an instant's time. In other words, "*what you want, when you want it.*"

Octavo, 1023 pages, with 145 engravings and 6 plates. By HOBART AMORY HARE, M.D., B.Sc., Professor of Therapeutics, Materia Medica and Diagnosis, Jefferson Medical College; Physician to the Jefferson Medical College Hospital; One-Time Clinical Professor of Diseases of Children, University of Pennsylvania. Cloth, \$5.50 net.

LUMB—Systematic Treatment of Gonorrhœa

*New Work
Just Ready*

A thoroughly practical handbook giving the practical details of methods of treatment found most valuable in thousands of cases. Covers Symptoms, Pathology and Bacteriology, Urinalysis, Routine Treatment, Special Treatment (Vaccines, Electro-Chemical, Mercury Compounds), Complications, Chronic Cases, Test of Cure, etc.

12mo, 119 pages. By N. P. L. LUMB, Captain, Royal Army Medical Corps. Cloth, \$1.50, net

706-8-10 Sansom St.
PHILADELPHIA

LEA & FEBIGER
PUBLISHERS

2 W. 45th Street
NEW YORK

Stanolind

Reg. U. S. Pat. Off.

Surgical Wax

A specially prepared, chemically pure, antiseptically-packed paraffin, for use in the hot wax treatment of burns.

Correct in melting point, in plasticity and ductility index.

Stanolind Surgical Wax is put up in quarter-pound cakes, individually wrapped in wax paper, carefully sealed, packed four cakes in a neat carton, and sold:

15c	per pound in	10 pound cases
14 $\frac{1}{2}$ c	per pound in	20 pound cases
14c	per pound in	40 pound cases
13c	per pound in	100 pound cases

Prices f. o. b. Chicago.

Reports from numerous authorities indicate that Stanolind Surgical Wax gives results equal to any of the compounds made and sold at high prices.

Stanolind Petrolatum

IN FIVE GRADES

"Superla White" is pure, pearly white, all pigmentation being removed by thorough and repeated filtering. Does not contain nor require white wax to maintain its color.

"Ivory White," not so white as Superla, but compares favorably with grades usually sold as white petrolatum.

"Onyx," well suited as a base for white ointments, where absolute purity of color is not necessary.

Compares favorably with commercial cream petrolatum.

"Topaz" (a clear topaz bronze) has no counterpart—lighter than amber—darker than cream.

"Amber" compares in color with the commercial grades sold as extra amber—somewhat lighter than the ordinary petrolatums put up under this grade name.

Standard Oil Company of Indiana guarantees the purity of Stanolind Petrolatum in all grades.

STANDARD OIL COMPANY

(Indiana)

Manufacturers of Medicinal Products from Petroleum

910 S. Michigan Avenue

Chicago, U. S. A.

Squibb's Mineral Oil
known as
Liquid Petrolatum
Squibb

Heavy (Californian)

Specially refined under our control, and exclusively for us, only by the Standard Oil Company of California which has no connection with any other Standard Oil Co.

FOR the Insane, Imbeciles, Patients in Coma, Hysterical Patients and all other cases of Irresponsibility, of Unconsciousness and of Altered Personality, Liquid Petrolatum Squibb is an efficacious and safe regulator of the bowels.

E. R. SQUIBB & SONS, NEW YORK
MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858



CORNELL UNIVERSITY MEDICAL COLLEGE

IN THE CITY OF NEW YORK

Holders of a Baccalaureate degree or Seniors who can present a degree before entering the Second Year, who also present the requisite courses in Chemistry, Physics, Biology, English and a Modern Language, are admitted from recognized Colleges and Scientific Schools. The Session opens on the last Wednesday in September. The first year is devoted to Anatomy, Chemistry, and Physiology and may be taken either in Ithaca or New York City. The last three years are chiefly Clinical and must be taken in New York City.

For further information and catalogue address—

THE DEAN, CORNELL UNIVERSITY MEDICAL COLLEGE,
Department C. First Avenue and 28th Street, New York City.

1918 PUBLICATIONS

- Cabot—Modern Urology.** Two octavo volumes of over 700 pages each, 649 illustrations. Cloth, per volume.....\$7.00
- Crotti—Thyroid and Thymus.** Imperial octavo, 570 pages, 96 engravings, 33 colored plates. Half Morocco, De Luxe.....\$10.00
- Aaron—Diseases of the Digestive Organs.** *New (2d) Edition.* Octavo, 818 pages, 172 illustrations. Cloth.....\$7.00
- Simon—Clinical Diagnosis by Means of Laboratory Methods.** *New (9th) Edition.* Octavo, 854 pages, 235 illustrations. Cloth.....\$6.00
- Vedder—Syphilis and Public Health.** 12mo, 315 pages. Cloth.....\$2.25
- McCombe and Menzies—Medical Service at the Front.** 12mo, 128 pages, illustrated. Cloth.....\$1.25
- Hare—Practical Therapeutics.** *New (17th) Edition.* Octavo, 1023 pages, 145 engravings, 6 plates. Cloth.....\$5.50 net
- Thornton—Pocket Formulary.** *New (11th) Edition.* Pocket size. Flexible Binding.....\$2.00
- Joslin—Diabetic Manual.** 12mo, 188 pages, illustrated. Cloth.....\$1.75
- Cushny—Pharmacology and Therapeutics.** *New (7th) Edition.* Octavo, 712 pages, 71 engravings. Cloth.....\$4.50 net
- Brown—Oral Surgery.** *New (3d) Edition.* Octavo, 734 pages, 570 engravings and 20 plates. Cloth.....\$7.00 net
- Treves—Surgical Applied Anatomy.** *New (7th) Edition.* 12mo, 702 pages, 153 illustrations, 74 in colors. Cloth.....\$3.00 net
- Gray—Anatomy.** *New (20th) Edition.* Imperial octavo, 1396 pages. 1247 large and elaborate engravings, many in color. Cloth.....\$7.50 net
Three-fourths leather..... 9.00 net
- Koplik—Diseases of Infancy and Childhood.** *New (4th) Edition.* Octavo, 928 pages, 239 engravings and 25 plates. Cloth.....\$6.00 net
- Bacon—Otology.** *New (7th) Edition.* 12mo, 583 pages, 206 illustrations. Cloth.....\$3.00 net
- Lumb—Systematic Treatment of Gonorrhoea.** 12mo, 119 pages. Cloth \$1.50 net

and.—THE WAR MANUALS

Make your Christmas selections from this list

706-8-10 Sansom St.
PHILADELPHIA

LEA & FEBIGER
PUBLISHERS

2 W. 45th Street
NEW YORK

NEW (4th) EDITION

DISEASES OF INFANCY AND CHILDHOOD

By **HENRY KOPLIK, M.D.**

Attending Pediatricist to the Mount Sinai Hospital; Consulting Physician to the Hospital for Deformities; Ex-President of the American Pediatric Society, etc.

**Octavo, 928 pages, with 239 engravings and 25 plates in color and monochrome
Cloth, \$6.00, net**

INTENSELY CLINICAL IN VALUE. Much new material will be found on acidosis; the infectious diseases, especially diphtheria, poliomyelitis and meningitis; syphilis; tuberculosis; diseases of the ductless glands and the blood—such as the Schick test, lumbar puncture, vaccine and serum therapy, neosalvarsan and mercuric treatment, glandular fever, septic infection; hemophilia, stomach lavage, etc. The sections on Nutrition and Infant Feeding and Nutritional Disturbances have been thoroughly revised and cover metabolism, breast feeding, artificial feeding (including the Rotch method and percentage calculations). Diet in disease and for children up to and after the sixth year receives careful attention.

Syphilis and Public Health

Just Ready

Invaluable to Practitioners and Public Health Officers for its masterly presentation of such vital points as Prevalence of Syphilis, with group statistics; Relation to Public Health; Sources of Infection; Methods of Transmission; Personal Prophylaxis against Genital and Extragenital Infection; Standard of Cure; Public Health Measures for Control of Venereal Disease—for Prevention of Syphilis; Technic of Wassermann, etc.

The book embodies what is actually known on the subject of Syphilis today, contains a very complete survey of the recent literature, and the important work done in experimental Syphilis and the prevention of the disease.

12mo, 315 pages. By EDWARD B. VEDDER, A.M., M.D., Lieutenant-Colonel, Medical Corps, U. S. Army. Cloth, \$2.25, net

Medical Service at the Front

Just Ready

A book by men who have been in the thick of it—Surgeon-General Fotheringham, D.G.M.S., Canada, says in his introduction "*It is hot from Hell's gridiron* and correct in all its details." It tells you the actual working system of the Medical Service—the Stretcher-Bearers' work following an offensive, the Advanced Dressing Stations in the dugouts of the trenches; the Field Hospital and factors governing selection of its site; the Evacuation Hospital, etc.; accompanied throughout by maps and diagrams which clearly indicate the disposition of the medical force in relation to the fighting corps.

12mo, 128 pages, with 25 illustrations. By Lieut.-Col. JOHN McCOMBE and Capt. A. F. MENZIES, C. A. M. C. Cloth, \$1.25.

706-8-10 Sansom St.
PHILADELPHIA

LEA & FEBIGER
PUBLISHERS

2 W. 45th Street
NEW YORK



THE BATTLE CREEK SANITARIUM AND HOSPITAL

Established 1866

MEDICAL
NEUROLOGICAL

OBSTETRICAL
SURGICAL

ORTHOPEDIC
RECONSTRUCTIVE

EDUCATIONAL DEPARTMENTS

Training School for Nurses

Normal School of Physical Education

School of Home Economics and Dietetics

Students received on favorable terms.

Registered trained nurses, dietitians and physical directors supplied.

DESCRIPTIVE LITERATURE MAILED FREE UPON REQUEST

THE BATTLE CREEK SANITARIUM
BATTLE CREEK Box 247 MICHIGAN

100% American

THE BAYER COMPANY, Inc., is controlled by the Alien Property Custodian and the manufacture and sale of its products are entirely under the supervision of **American Officers and Directors** appointed by him.

As soon as its books have been audited and the property appraised, the capital stock of the Company will be sold by the Alien Property Custodian to **American Citizens**.

All profits as well as all the money realized from the sale of the Company will be used for the purchase of Liberty Bonds to help in the prosecution of the War until the **complete defeat of Germany**.

Therefore, genuine **Bayer-Tablets and Capsules of Aspirin** as well as other **Bayer products** can be purchased with full confidence.

THE BAYER COMPANY, Inc.

117 HUDSON STREET

NEW YORK, N. Y.

RADIUM INSTITUTE

Radium Sanatorium of New York

205 WEST 70th STREET

NEW YORK

PHONE—COLUMBUS 7021

An institution for the treatment of malignant and benign growths with radium and allied measures of therapy. Adequate amounts of radium are available to meet all the requirements of dosage.

Standard operating rooms open to all surgeons of good standing. Post-operative radiation may be arranged for either at the Institute or at other hospitals.

Radio-active waters, in any mache unit strength, delivered on physician's prescription—Indicated in arterio-sclerosis, arthritis, and manifestations of the senile period. Consultation with the Directors should be arranged for before bringing patients to the institution.

JOSEPH B. BISSELL, M.D.
Surgical Director

C. EVERETT FIELD, M.D.
Managing Director

PROCAINE

A Local Anesthetic

Chemically Identical with Novocain

In 1917, when no American concern was making this drug, and the German manufacturers had prohibited the sale of their product to our allies, this Company placed its resources at the Government's disposal and agreed to produce PROCAINE for the United States.

Ten thousand bottles of PROCAINE went to the Navy, over ten thousand ounces to the Army, besides over a million tablets. We have also supplied the needs of the Red Cross, hospitals and the Medical and Dental professions.

All this was accomplished without German help, by American born and trained chemists.

RECTOR PRODUCTS ARE 100% AMERICAN

When ordering PROCAINE, insist upon PROCAINE made by

RECTOR CHEMICAL CO., Inc. - - 2 Rector St., New York

1871

R
11
A5
n.s.
v.156
cop.2

The American journal of the
medical sciences

Biological
& Medical
Serials

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY

STORAGE

