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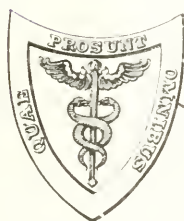
OF THE
MEDICAL SCIENCES

EDITED BY
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VOL CLIX



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M Osler

WILLIAM OSLER.

A GREAT physician, a wise counsellor, a true man and above all a friend has gone to his long home. William Osler is dead. There is no man in the profession in any land whose passing could bring sorrow and a keen sense of personal loss to so many. It is a far cry from the rectory in Tecumseth, Ontario, in 1849, to Oxford in 1919; but the journey never seemed long to him, for he travelled cheerfully, did each day's work as it came and never lost a chance of helping others. His philosophy of life was simple—to do the day's work well and not trouble about the morrow, to act the Golden Rule and to cultivate a spirit of equanimity. Many other qualities were evident in his daily life; two stand out, kindness and the habit of charity toward all men. His darkest days came when his son gave his life in France, but he bore the sorrow with fortitude and kept on with his daily work—"Carry on" was the word. His work during the war was very heavy, and he was constantly laboring to the limit of his strength.

How can one state his many activities in a few words? Professionally he did much to advance knowledge, to improve medical education and to uphold the best traditions of a profession which he loved. A friend of young men, he never missed the opportunity to encourage and help them. How often he sent an approving word about an article or a good piece of work. As a teacher he did much to help medical education in this country and taught the lesson that the knowledge of disease is to be learned at the bedside rather than in the lecture room. A lover of books, he gave the first stimulus to many of an interest in literature, and especially in medical history. As a physician he inspired confidence and gave courage to the sick with a constant example of kindness and consideration to those about him.

He put his mark on medicine and men wherever he lived and worked. There are men in Philadelphia who show the influence of his teaching there over thirty years ago. Much of the success of the Johns Hopkins Hospital and Medical School is due to him. To the profession he gave freely of time and advice. His influence was always exerted to promote "Unity, Peace and Concord." For him the general practitioner was the backbone of the profession. He would never listen to any word said in detraction of a brother practitioner.

There were other activities. His knowledge of literature was extensive and in him the Greek philosophers had an eager student. For one without a special training his classical knowledge was remarkable. His essays take no mean place both in matter and style. But after all, what we think of most is the humanness of the man—"Homo sum; humani nihil a me alienum puto." He met the ignorant and the wise and both could learn from him. That he did so much was a constant wonder, but he knew the value of minutes and had the art of concentration. Of his kindness to others one learned only by chance; many of the readers of this know of his kindness to them.

Cheerfulness was a characteristic; work with him was never dull. He never had to unbend, and where he sat was the head of the table. What a fund of reminiscence and incident he had and how naturally and easily he could draw on it. The opportunity for a jest was rarely lost, but the jest was a kindly one. A wound was rarely felt by the one at whom the arrow was shot. But how his lighter doings and sayings puzzled some of his acquaintances—not his friends, for they understood.

To those who worked with him in Baltimore many memories come back of the days in the hospital and classroom. No man ever had more devoted assistants; to them he was "The Chief," and that title in their thoughts can never belong to anyone else in the sense that it did to him. The alert, active figure entering the hospital a few minutes before nine, and always on time, the ward rounds, the hunt in the library for an article, the discussion of some special point, the interest of the clinic, are part of the recollections that come back. For his students the Saturday evenings at his home must stand out as perhaps the best hours of their undergraduate life.

Now we have the memories only, but they are precious ones. For many of us William Osler stands as the strongest influence in our lives. He will be missed and mourned, but his influence goes on and generations of medical students yet unborn will profit by his life and work. From his passing there will be for many an added meaning to the words of Milton:

But O the heavy change, now thou art gone,
Now thou art gone, and never must return!

THOMAS McCRAE.

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ORIGINAL ARTICLES

SOME PRACTICAL POINTS IN PROSTATIC SURGERY.¹

BY JOHN B. DEAVER, M.D.,

PHILADELPHIA.

THE mortality rate following prostatectomy is in direct ratio to three vitally important factors: (1) The recognition of absolute contra-indications to operation; (2) the recognition of relative contra-indications to operation, and (3) the knowledge of methods of treatment preliminary to operation that will remove such relative operative contra-indications and thus bring the individual within the operable class.

Characteristic illustrations of these factors are most frequently found in subnormal function of the kidneys. In one instance an impending uremia may be due solely to an antecedent nephritis of the chronic interstitial type, in which event, the cause being irremovable, there is an absolute contra-indication to operation. In another instance a minor degree of interstitial nephritis may exist, but the dangerously low renal function present is dependent upon back pressure incident to lower urinary obstruction. Under these circumstances there is a relative contra-indication to operation, because after decompression of the kidneys the renal function improves, so that eventually the obstructing prostate can be removed successfully.

Similar relative contra-indications occur as the result of altered kidney function, consequent upon decompensation of the cardio-

¹ Read before the Buffalo Academy of Medicine, Buffalo, N. Y., November 5, 1919.

vasomotor systems. With proper treatment the blood-vascular tone may improve and coincident with it the renal function is restored. Such restoration of function could obviously be accomplished in no other way in cases of this kind than by treatment of the cardiovascular system.

In a small proportion of cases an obviously enlarged prostate may be accused of giving rise to symptoms and conditions for which it is only partially or even not at all responsible. Mistaken diagnoses of this kind are almost invariably due to lack of completeness in the physical examination, and especially of the nervous system. In an individual with early tabes and an enlarged prostate gland the symptoms of prostatism may be due chiefly to bladder atony resulting from the cord lesion. This constitutes an absolute contra-indication to prostatectomy. In other instances removal of the prostate is indicated, but only after it has been definitely established that the symptoms are due in major part to its enlargement. The tabetic lesion constitutes a relative contra-indication, in that specific treatment is advisable before removal of the prostate is attempted. In many instances the differentiation between absolute and relative contra-indications is a most difficult, if not impossible, matter. We cannot reproach ourselves for the mortality following prostatectomy in those cases in which every attempt has been made to make this differentiation, but in which the contra-indications which seem to be relative were, as events proved, absolute once.

In only a small proportion of cases does the primary examination reveal complications that absolutely preclude the possibility of operation. The majority of complicating factors that would result in a fatality with immediate operation are so far removable that prostatectomy can be performed later in comparative safety. The success of the individual surgeon is far more dependent upon his ability to recognize and treat relative contra-indications, together with the selection of the proper time for operation, than upon his technical skill in removing the obstruction.

The general mortality rate of prostatectomy throughout the country is well above 20 per cent., and 69 per cent. of all deaths following the operation are caused by uremia, hemorrhage, shock and sepsis. In a collected series of 147 cases of the immediate postoperative death, uremia was given as the result in 39 instances, hemorrhage in 32, shock in 18 and sepsis in 13. Practically the same mortality rate is attributable to uremia and sepsis as is given for hemorrhage and shock. In other words, about half of the operative mortality dependent upon the major causes of operative death follow complications that existed as relative contra-indications before operation; the remaining deaths are directly dependent upon technical complications of the operation. If we include other causes of death, such as asthenia, infected kidney, etc., with the group that presented preoperative contra-indications, the percentage of deaths due to

failure to recognize the danger signals will be materially increased. It is difficult to realize that almost as many prostatectomy deaths are due to hemorrhage as to uremia, but such is the fact. It is necessary to recognize and to treat properly the relative contra-indications to prostatectomy and to so perform the operation that fatal hemorrhage and sepsis will be rare events, instead of the extraordinarily common ones which they are at the present time if the mortality of prostatectomy is to be reduced.

Absolute contra-indications to the removal of the benign hypertrophic prostate are frequently encountered; that they are too often disregarded is evident from the existing mortality rate. The relative contra-indications are presented in the vast majority of cases; here, again, the high mortality rate bespeaks the indifference of many operators to dangerously low functional activity of vital organs. One of the rarely admitted absolute contra-indications to operation is the inability of the surgeon to control hemorrhage or to remove the prostate within limits of traumatic injury that the patient is able to bear.

The absolute organic contra-indications generally affect groups of organs rather than a single organ, although the major symptomatology will often direct attention, especially to one or other organ or system. An exceedingly high blood-pressure, for instance, in an aged individual is usually indicative of cardio-arterial pathology, but in some instances it is largely compensatory to interstitial nephritis. When purely compensatory in type a failure in compensation may occur after prostatectomy, owing to the added strain thrown upon the kidneys. Nature may fail in her attempts to further increase the blood-pressure so as to insure renal function, or, having successfully accomplished this, a cerebral vessel may burst or the heart may suddenly dilate, with death following in either event. In the absence of these fatal factors death may occur from renal failure, notwithstanding a better cardiovascular function after operation than before. High arterial tension in itself is not a positive contra-indication to operation, but a cardiovascular system which shows no elasticity in function after the institution of treatment designed to relieve the causes of high arterial tension is not dependable, and if, in spite of the maximum compensatory activity of the cardiovascular system the renal function, despite treatment, is barely sufficient it is worse than foolhardy to attempt prostatectomy. A decompensated cardiovascular system which does not respond to treatment obviously contra-indicates operation. Impending uremia commonly delays operation but does not necessarily preclude it. We are realizing more and more how really few prostatics have kidney defects which cannot be removed or at least relieved sufficiently to make the individual safe for prostatectomy.

In our experience sepsis and toxemia productive of a general low ebb vitality are frequent contra-indications to operation. In these

cases a low-grade uremia is often a chief contributing factor, but this is not always true. We refer now to the individual prematurely aged as the result of excesses, the victim of manifold chronic toxemias whose vitality is further sapped by chronic sepsis of bladder and kidney origin. These individuals are anemic, their tissues are flabby, their appetite is poor and their resistance nil. The renal function in this class of patients may be relatively normal and the most careful examination may fail to reveal any positive contra-indication to operation; yet we know from experience that these patients die after prostatectomy from causes that are grouped under the term asthenia. After weeks or months of the most careful treatment many of these patients can be safely operated upon; to operate them without such preliminary treatment is inexcusable.

Renal failure is by far the commonest contra-indication to operation, but it is usually a relative contra-indication. It is our duty to determine the degree of renal impairment and the possibilities of its improvement under treatment. The surgeon must familiarize himself with the various methods of measuring renal function and of selecting and applying methods of treatment best suited to restore this function, and, finally, he must be able to recognize maximum renal function and to judge correctly the ability or inability of the kidneys to support life after prostatectomy. Surgical success in these cases, above all others, depends upon the abilities of the surgeon as a physiologist.

We are fortunate in having many means of estimating renal function—our misfortune lies in not possessing any other method that will accurately measure the function of the kidneys in every instance. It is only by repeated examinations and weighing the evidence furnished by many tests that one can accurately gauge kidney function, especially as regards the reserve capacity of these organs. The tests of retention, of which the most important is the blood-urea test and the tests of excretion, of which phenolphthalein is the most accurate, usually give similar results. This is by no means the invariable rule, however, and on account of these exceptions the tests of excretion are sometimes condemned. To condemn these or any other tests because of exceptional failures is unfortunate, inasmuch as they are capable, when properly interpreted, of giving much valuable information. It is likewise a mistake to pass one's opinion on a single test, inasmuch as the tests of excretion are indicative only of the function of the kidneys during a specific interval of time. A single test of retention is more to be relied upon than a single test of excretion. Urea in the blood is the ash of protein derivatives and in the absence of tissue obstruction is derived almost entirely from the food. Furthermore, it is a threshold substance which is taken from the blood by the kidneys when the normal concentration is exceeded. Therefore, renal failure promptly gives rise to urea retention. This rule, too, is not

without exceptions, and in certain instances an impending uremia may exist though the blood urea is only slightly if at all increased.

A concentration of urea, 0.5 gm., and of the total incoaguable nitrogen, 0.6 gm. per liter of blood, has been the accepted normal level, but Folin and Davis have found that a concentration of non-protein nitrogen 26 mg. and urea nitrogen 13 mg. per 100 gm. of blood is normal. Concentrations of less than 0.6 gm. of urea per liter of blood are of little prognostic significance in our experience. The results of the blood-urea test are always contrasted with the pthalein excretion. A low pthalein output, 20 per cent. or less, is usually but not always associated with retention of urea. If a low pthalein excretion and urea retention occur together the renal function is certainly greatly impaired; operation should be withheld until these results are confirmed or disapproved by repeated tests. If, on the other hand, a low pthalein output is not associated with urea retention and the general condition of the patient is good, we are prone to disregard the results of the pthalein test. Again, a high percentage output of pthalein is not incompatible with dangerous urea retention. These are exceptional cases, however, and they are certainly not good reasons for discarding so valuable a procedure as the pthalein test. We are prone to forget the old-time tests of renal function. Their very simplicity no doubt condemns them to forgetfulness. I refer to the quantity of the urine and to its specific gravity. As a rule the results of the kidney function tests indicate an altered state of function which Nature has expressed in the production of a urine low in content of solids, and therefore low in specific gravity, but often great in quantity. We have, however, seen cases in which the various functional tests indicated a good state of renal function but in which the urine was abnormally low in specific gravity. I personally would refuse operation in any individual whose urine showed a specific gravity persistently below 1005, regardless of the results of any functional tests. No fear of uremia need be entertained for the individual whose kidneys secrete a normal quantity of approximately normal urine. The quantity of urea in the urine is of little prognostic significance, except it be compared with the quantity of blood urea; we believe that Ambard's constant is of value and should be taken advantage of in clinics where laboratory facilities are at hand for its estimation. It is important that the urine be studied for acetone and diacetic acid. Acidosis is a factor to be reckoned with therefore every precaution to prevent as well as to correct it when it occurs.

Cultures of the urine are made in all our prostatic cases, since we believe it is important to know the type of infecting microorganisms present. This enables us to intelligently guide the preoperative treatment, especially as regards the length of time necessary to continue preliminary drainage of the bladder. It is also of assistance in determining whether preliminary cystostomy should be done,

and if so, what type of local treatment is to be employed and how long it should be continued. Sensitized bacterins are occasionally of value in helping to overcome the infection, especially in the presence of a complicating pyelitis.

Practically all of our patients are cystoscoped, but not until they are subjected to preliminary treatment. The bowels should be freely opened with a saline cathartic. Copious drinking of water should be encouraged and formin and acid sodium phosphate administered for several days at least before the cystoscopic examination is made. The cystoscopy is absolutely essential in certain cases of hematuria for the differential diagnosis of benign from malignant prostate or in the recognition of a complicating papilloma. The size and shape of the intravesical portion of the prostate is determined cystoscopically as well as bladder complications, such as stone and diverticulum. Vesical diverticulae are important causes of morbidity following prostatectomy. A pouch of this nature in communication with the bladder cavity will give rise to the symptoms of prostatism, and if the patient is informed of the probable necessity of a second operation for its removal the surgeon will be spared much embarrassment when the removal of the prostate fails to remove the symptoms.

Low renal function in prostatitis is not infrequently dependent upon surgical kidney, so that differential studies of kidney function are sometimes necessary. In these cases we prefer the indigo-carmin test. This test is particularly applicable to prostatic cases on account of the ease and rapidity with which it may be performed.

Catheterization of the ureters, which is often difficult and sometimes impossible in the presence of large intravesical projections, is unnecessary. Obviously this test lacks the exactness and refinement of differential phthalein studies, but it serves for all practical purposes in prostatic cases in which differential studies are necessary.

PRELIMINARY TREATMENT. Practically all prostatitis are in need of treatment before operation can be safely undertaken. In certain cases of acute retention, prolonged and unsuccessful attempts to insert a catheter have so traumatized the urethra that further attempts to relieve the patient instrumentally are unjustified. Under these circumstances the bladder should be drained suprapubically. The bladder may be explored with the finger at this time and any calculi should be removed. In desperate cases in which the retention has continued for a long time and the bladder has become greatly overdistended the sudden relief of intravesical pressure is extremely dangerous. Formerly we employed the trocar in cases of this kind, but probably a better procedure is the introduction, under local anesthesia, of a female retention catheter. The bladder is exposed suprapubically, the bulb of the catheter is

folded and grasped in the jaws of a pair of dressing forceps and is introduced through a very small incision into the bladder. The tube is clamped off and traction is put upon it so that the bulb of the catheter fits snugly against the bladder mucosa. If too large a single stitch will serve to close the incision tightly around the catheter. This procedure can be carried out with the loss of little if any urine. By removing the clamp from the tube at intervals the bladder may be emptied intermittently. This does away with great danger, due to sudden and complete emptying of the bladder. Under ordinary circumstances we prefer a drainage tube of large caliber, but in cases of long-continued complete retention which cannot be relieved *per urethram* I am sure that the above procedure is a life-saving measure. Long-continued drainage of the bladder, which is usually necessary in these cases, can be accomplished in this manner most effectively and without discomfort to the patient incident to the prolonged leakage of urine. This is the only type of case in which it is necessary to operate immediately, and primary prostatectomy is attended by approximately 100 per cent. mortality in this group.

If the urethra is patulous we prefer the indwelling catheter in the initial stages of treatment in most cases, but under other circumstances, preliminary cystostomy should be performed without delay.

In draining the bladder suprapubically, as the first stage of a two-stage prostatectomy, we prefer, as we have just mentioned, a drainage tube of large caliber. This is especially indicated when cystitis is a prominent complication. Prolonged drainage is essentially necessary in cases in which extensive ecchymosis of the bladder mucosa has occurred. This condition is easily recognized by the chocolate-coated appearance of the mucous membrane, an appearance which is due to intramucosal and submucosal hemorrhages. The bleeding is the result of the local action of bacterial toxins. The mucosa becomes softened, thickened and irregularly stained by reduction substances derived from the hemoglobin, which give to the membrane its chocolate-coated appearance. This condition may, but rarely does, give rise to hematuria. The altered mucosa is much more absorbative than is the normal mucous membrane of the bladder, which fact explains the chronic toxemia from which these patients suffer. In this fact also we find the *rationale* for drainage of the bladder for a sufficient period to permit regeneration of the mucosa to take place.

Preliminary cystostomy, more than any other single procedure, has materially reduced the operative mortality of prostatectomy. We do not employ it routinely, however. In early cases of prostatic enlargement, that is, in patients with small amounts of residual urine, patients whose kidneys are functionally satisfactory and in whom there are no definite contra-indications to operation we prefer to remove the prostate without preliminary drainage of the

bladder. In the majority of cases the catheter is used either intermittently or constantly, and if the kidney function and general condition improve sufficiently, we proceed at once with the prostatectomy. In the remaining group of cases, which includes all those in whom the preliminary catheter treatment has failed, we advocate the two-stage operation.

There are certain technical difficulties associated with the removal of the prostate, which are dependent upon preliminary drainage of the bladder—difficulties which cannot easily be overcome. The size of the incision is limited to the distance between the drainage opening and the pubic bone, since it is unsafe to enlarge this incision upward on account of the danger of opening the peritoneal cavity, the peritoneum having become attached to the bladder wall in the line of the original incision. This gives insufficient exposure of the prostatic bed, and in the event of hemorrhage it is often difficult to apply gauze packing. This is the one certain way to control hemorrhage after prostatectomy. Distensible bags and similar playthings are effective only in cases in which there is no bleeding.

Very large prostates are usually easily enucleable, but it is frequently quite difficult to deliver them through the small suprapubic wound; in fact, it is frequently necessary to section the gland and remove it piecemeal.

Preliminary drainage of the bladder serves, however, to relieve the congestion of the prostate gland, so that at the time of the second stage of the operation it is much smaller than the digital examination at the time of the first operation would lead us to believe. This shrinkage of the organ, while serving to add to the difficulties of enucleation, minimizes postoperative bleeding, so that packing to control hemorrhage is less often necessary with the two-stage operation. The success of prostatectomy, let me repeat, is chiefly dependent upon the preliminary treatment; of secondary importance are the technical details with which the enucleation of the prostate is accomplished.

SURGICAL RENAL TUBERCULOSIS: THE PROGNOSIS.¹

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SEVERAL factors affecting the prognosis in cases of surgical renal tuberculosis have not as yet been definitely determined. Probably the most important of these are: Age, sex, coincident tuberculosis in other tissues, duration of symptoms, degree of involvement of the bladder and kidney and bilateral renal disease.

¹ Presented before the American Association of Genito-Urinary Surgeons, June, 1919, Atlantic City.

According to the surgical records of the Mayo Clinic 532 persons were operated on for renal tuberculosis from January 1, 1894, to January 1, 1918. During this period about 85,000 patients were operated on; thus the incidence of surgical renal tuberculosis may be estimated as 0.6 per cent. A previous review² has been made of the postoperative records of a portion of these cases, but the present data have been derived from more complete records and a larger number of cases.

The total number of patients (532) was employed in the estimation of many of the general statistics. Among this number were 16 patients who were known to have bilateral renal tuberculosis and were therefore not considered in the survey of postoperative results. Statistics bearing on postoperative results were based on the postoperative records of patients heard from either by correspondence or by personal examination. This number included 435 patients (81.3 per cent.) of those operated on. It will be noted that only the postoperative records of patients operated on prior to January 1, 1918 were studied. In considering the influence of the different complications it was found that more detailed data were available in 346 cases in which operations were performed from January 1, 1912, to January 1, 1918 inclusive.

TABLE I.—AGE.

Patients operated on 532		
2 patients	0 to 10 years	0.4 per cent.
37	11 to 20 "	6.9 "
197	21 to 30 "	37.0 "
168	31 to 40 "	32.0 "
89	41 to 50 "	16.7 "
36	51 to 60 "	6.7 "
3	61 to 70 "	0.6 "

Patients with post-operative data, 435.

		Reported dead.
32 patients	11 to 20 years	9 (28.1 per cent.)
161	21 to 30 "	41 (26.2 "
137	31 to 40 "	26 (18.9 "
75	41 to 50 "	20 (26.6 "
27	51 to 60 "	7 (25.9 "
3	61 to 70 "	1 (33.3 "

The greatest incidence of surgical renal tuberculosis (69 per cent. of the total) occurred between the ages of twenty and forty. The largest number of cases (37 per cent.) is in the third decade. The condition is rarely found in the first and seventh decade. When tuberculous infection of the kidney does occur in children, it is usually in conjunction with tuberculosis disseminated in other tissues so that operation is inadvisable. Nephrectomy in children should not be done with the first onset of symptoms; it is advisable only

² Braasch, W. F.: Clinical observations from 203 patients operated on for renal tuberculosis, Jour. Am. Med. Assn., February, 1912, lviii, 397-401.

when it is evident that the active tuberculous infection is localized to the kidney.

The influence of age on the ultimate prognosis is of comparatively little significance and the general mortality average remains fairly constant in the various decades. The late mortality during the third decade is somewhat lower than that during the other decades, but the difference is not great enough to warrant any definite prognostic distinction. In the first and last decades too few cases are involved to give the mortality percentage any accurate value.

TABLE II.—SEX.

Patients	532
Males	338 (63.5 per cent.)
Females	194 (36.5 " "
Patients with postoperative data	435
Deaths	105
Males	75 (27.5 " "
Females	30 (18.4 " "

The greater number of male patients is in keeping with the preponderance of male patients in cases of other chronic infections of the kidney. The relative mortality is somewhat higher in the male. The relative duration of preoperative symptoms is practically the same in both sexes.

TABLE III.—COINCIDENT LESIONS.

Patients with renal tuberculosis operated on from 1912-1918	346
" with coincident lesions	244 (71.0 per cent.)
" with complete postoperative data	201
" who died	33 (16.4 " "
" with one lesion	89
" with one lesion who died	14 (15.7 " "
" with two lesions	56
" with two lesions who died	9 (17.8 " "
" with three lesions	39
" with three lesions who died	5 (12.8 " "
" with more than three lesions	17
" with more than three lesions who died	5 (29.4 " "

Evidence of tuberculosis in other parts of the body, either healed or active, was found in 244 of the 346 patients (71 per cent.) operated on since 1912. In the examination of a patient with suspected renal tuberculosis a thorough search for such complications is necessary. In fact, it is questionable whether renal tuberculosis ever occurs without coincident tuberculosis in some other tissue, and which may not be apparent on casual examination. That such complications exert but little influence on the ultimate prognosis is evidenced by the fact that the mortality percentage in our cases was even lower when coincident tuberculosis was noted than that of the general average. The occurrence of coincident tuberculosis, particularly when healed or dormant, does not necessarily render the prog-

nosis less favorable: in fact, it may be regarded as an evidence of good resistance power on the part of the patient. In reviewing the postoperative results of the patients with complications, it is of interest to note that when multiple lesions occurred the percentage of recovery was relatively as great as when only one lesion was noted. The only exception occurred when multiple, active complications existed as a part of a generalized tuberculosis. The individual influence of the various coincident tuberculous lesions will be considered separately.

TABLE IV.—COINCIDENT PULMONARY TUBERCULOSIS.

Patients operated on for renal tuberculosis 1912-1918	346	
“ having complete postoperative information	298	
“ who died	44 (14.7 per cent.)	
“ having complete x-ray and clinical examination of chest	300	
“ having definite evidence of pulmonary involvement	81 (27.0 “	
“ having definite active tuberculosis	16 (5.3 “	
“ having definite active tuberculosis and complete postoperative information	13	
“ who died (none in hospital)	6 (46.3 “	
“ having doubtful active tuberculosis	17	
“ having doubtful active tuberculosis and complete postoperative information	16	
“ who died	3 (18.7 “	
“ having definite healed tuberculosis	26	
“ having definite healed tuberculosis and complete postoperative information	21	
“ who died	2 (9.5 “	
“ having indefinite clinical or indefinite evidence of previous pulmonary involvement	22	
“ having complete postoperative information	19	
“ who died	1 (5.2 “	

Pulmonary tuberculosis is one of the most common complications occurring with renal tuberculosis. Fortunately, it is usually found in a chronic or healed form. Renal tuberculosis is not a common complication of active pulmonary tuberculosis. It occurred as a coincident infection in less than 5 per cent. of our patients. As a part of a general or a miliary tuberculosis the coincident infection probably occurs more frequently. Pulmonary tuberculosis as a secondary complication of renal tuberculosis is of relatively infrequent occurrence, although it is a factor in the late mortality after nephrectomy.

Complete roentgen-ray and clinical examinations were made of the chest in 300 patients. Evidence of pulmonary tuberculosis was found in 84 (28 per cent.). The cases were divided into four groups: (1) Definite active tuberculosis; (2) doubtful active tuberculosis; (3) definite healed tuberculosis, and (4) doubtful clinical or roentgen-ray evidence of previous involvement. A number of patients in whom the physical and roentgen-ray data were indefinite were not included.

In Group 1 were 16 patients (4.6 per cent.) of the total number operated on. Fourteen were males and 2 were females. The mortality of this group, as might be expected, was very high; 6 (37.5 per cent.) of the patients died. However, since almost two-thirds of the patients recovered it is evident that active pulmonary tuberculosis does not necessarily exclude operation in cases of renal tuberculosis, but, on the contrary, offers a fair chance for recovery. In the majority of these cases the active pulmonary lesion was confined to comparatively limited areas, diffuse miliary involvement being regarded as excluding operation. In several cases, although the lesions were quite extensive and even bilateral, the general condition of the patients warranted operation. In several cases of well-advanced pulmonary tuberculosis the advisability of operation was doubtful, but it was rightfully argued that an operation offered the only chance of recovery. The most important factor in determining the advisability of operation was the patient's general condition. None of the patients died in the hospital or immediately following operation, showing that the anesthetic (ether in every case), even in the presence of active pulmonary tuberculosis, had no immediate harmful effect.

Group 2 probably includes a small number of patients with limited active lesions. The mortality was approximately average. In Groups 3 and 4 the mortality was unusually low. From this it may be argued that patients with healed pulmonary tuberculosis have developed high resisting powers against the tuberculous infection, and that complicating renal tuberculosis is an evidence that the resistance of patients is only temporarily lowered at the time of the renal infection.

TABLE V.—GENITALIA.

Male patients operated on (1912-1918)	234
Lesions in genitalia	171 (73.0 per cent.)
Complete postoperative data	141
Reported dead	26 (18.4 " "
Epididymectomy prior to operation	26
Epididymectomy after operation	24
Patients who died following epididymectomy after operation	3 (12.5 " "

Coincident tuberculosis in the genitalia rarely occurs in the female; it was noted as definite in 171 (73 per cent.) of the group of 234 male patients. Twenty-six of these patients (18.4 per cent.) died, 13 during the first year. The late mortality is therefore not greatly influenced by this complication. The high percentage of recoveries among the patients in this group who had clinical evidence of tuberculosis in the prostate and seminal vesicles should contra-indicate surgical treatment of these organs. It is evident that spontaneous healing must occur in the majority of instances. On subsequent examinations the prostate and vesicles are usually diminished in size, and either hard and fibrous or apparently practically normal.

Acute suppuration in the prostate and seminal vesicles is unusual. Surgical treatment of the tuberculous prostate is indicated only in certain cases of protracted vesical irritation or in the presence of suppuration.

Tuberculosis in the epididymis and testicle should be treated surgically because of the frequency of suppuration and because the process does not usually become dormant and disappear. Furthermore, a tuberculous epididymis must always be regarded as a possible focus of general infection. Epididymectomy was done in 50 patients in the series, 26 prior to nephrectomy and 24 following nephrectomy. Three (12.5 per cent.) of the last group are reported dead.

TABLE VI.—BONES AND JOINTS.

Patients with lesions	21 (6.0 per cent.)
Patients with complete postoperative data	19
Patients with lesions described as active	10 (57.8 “
Patients reported dead	1 (5.2 “
Patients with spondylitis	17 (5.7 “
Patients with active spondylitis	3
Patients reported dead (1 active spondylitis)	2 (11.7 “

Tuberculosis, either healed or active, involving the bones and joints, is not unusual with renal tuberculosis. A review of our records shows 21 (6 per cent.) such cases. Of this number 10 were described as active. Four (13.3 per cent.) of the patients are reported dead. Coincident lesions in the bones, even though active, have little or no bearing on the prognosis, provided it is not a part of general acute tuberculosis.

To the group of complications involving the bones should be added the cases of spondylitis. Fourteen patients were suffering with chronic and three with active spondylitis. Two of the former and one of the latter are reported dead, evidence that chronic spondylitis does not greatly affect the ultimate result. Active spondylitis, particularly in the presence of other tuberculous lesions, will necessarily make the prognosis much more serious, but it does not contraindicate operation. One of the patients with an active process operated on six years ago is living, in a fair degree of health. In a number of such patients observed the condition was regarded as inoperable either because of their general health or the presence of other active complications.

ADENITIS.

In but 19 (6.4 per cent.) patients was there any well-marked evidence of tuberculous adenitis. In the majority of these only a few glands were involved, and in none sufficiently to require surgical intervention. Two of the nineteen patients (10 per cent.) are reported dead, indicating that this complication has no bearing on

the prognosis other than to show the high resistance on the part of the patient.

TABLE VII.—HEMOGLOBIN.

Patients having less than 80 per cent.	73
Patients reported dead	7 (9 per cent.)
Average duration of bladder symptoms (2 cases without)	2 yrs. 9 mos.
Patients with 50 per cent. or below (one died)	8

Anemia secondary to renal tuberculosis is frequently noted. Its incidence in our series was 25 per cent. As a rule the degree of anemia is not marked. The reduction in hemoglobin is seldom caused by the loss of blood from hematuria. It is not in proportion to the duration of symptoms of the bladder, since a number of patients with low hemoglobin had symptoms of only a few months' duration. The average duration was two years and seven months, which is about the average of all cases. The greatest reduction of hemoglobin is noted with extensive renal suppuration when absorption of toxins was evidently the cause. The degree of hemoglobin gives no index to prognosis; 8 patients had 50 per cent. hemoglobin, or below, of whom 1 died. Seven patients in the series (9 per cent.) are reported dead.

TABLE VIII.—BLADDER INVOLVEMENT.

	Patients.	Dead.	Per cent.
Degree 1	55	8	14.5
Degree 2	92	9	9.7
Degree 3	71	16	22.5
Degree 4	43	7	16.2

The pathological condition in the bladder as noted on cystoscopic examination in this series is estimated on a scale of 1 to 4; 1 slight involvement; 2 moderate; 3 marked, and 4 extreme. It was found that the patients were about equally divided between moderate (1 and 2) and marked (3 and 4), the largest single group being 3. The average duration of preoperative symptoms when the degree of inflammation was scaled 3 and 4 was two and one-half years, and when it was scaled 1 and 2 it was only one and one-half years. When the preoperative degree of bladder inflammation was slight or moderate (1 and 2) it was found that immediate postoperative improvement in bladder symptoms occurred in 20 per cent., whereas with bladder inflammation graded 3 and 4 immediate improvement was noted in only 10 per cent. The late mortality in cases of moderate bladder involvement (1 and 2) was practically 11 per cent., whereas with advanced involvement (3 and 4) it was 20 per cent., or twice as great. Although the renal disease usually has existed longer in cases of marked bladder involvement, the difference in involvement is evidently more dependent on the virulence of the infection than on the duration of symptoms.

TABLE IX.—DEGREE OF PATHOLOGY.

Patients with complete postoperative data (1912-1918)	298
Patients dead	44 (14.7 per cent.)
Patients with limited lesion	37
Patients dead	2 (4.5 "
Patients with advanced lesion	159
Patients dead	25 (15.7 "
Patients with large pyonephrosis	58
Patients dead	12 (20.6 "
Patients with occluded tuberculosis	44
Patients dead	5 (11.3 "

The conditions of the kidneys removed were divided into four groups: (1) Slight lesions; (2) advanced lesions; (3) complete destruction, described as advanced pyonephrosis; and (4) occluded (caseated) tuberculosis. The lesions in the first group were slight, consisting of limited single areas or multiple early lesions. The mortality in this group (4.5 per cent.) was the lowest and seems to refute the necessity of the patient's development of immunity before the kidney is removed. In by far the largest number of patients the pathological condition of the kidneys was described as advanced (Group 2). Multiple areas involving from one to two-thirds of the kidney substances were usually found. In Group 3 the process has generally existed for so long a time that extensive suppuration has occurred. The mortality is greatest and is probably explained by absorption of toxins from the extensive abscesses, with consequent damage to the other organs. Nevertheless, the most gratifying results are frequently obtained among patients in this group who before their operation are often in extremely poor general condition and afterward become quite normal. Group 4 is in reality a group by itself. It is composed of patients in whom Nature has occluded the ureter, performing a so-called autonephrectomy, and the tuberculous process is supposed to have run its course. In only a few such cases was there any evidence of active tuberculosis in the kidneys; in the majority, the original kidney tissue had undergone caseation. The low mortality is evidenced by the patient's high resisting powers.

TABLE X.—DURATION OF PREOPERATIVE SYMPTOMS.

Cases.	No change or slight improved.	Markedly improved or practically well.	Dead.
1 to 3 months	30 (13.3 per cent.)	18 (60.0 per cent.)	8 (26.6 per cent.)
4 to 12 months	162 33 (20.3 "	87 (53.7 "	42 (25.9 "
1 to 5 years	155 40 (25.8 "	71 (45.8 "	44 (28.3 "
5 years	57 23 (40.3 "	27 (47.3 "	7 (12.2 "
Indefinite	31 4 (12.9 "	23 (74.1 "	4 (12.9 "
Total	435 104 (23.9 "	226 (51.7 "	105 (24.1 "

The influence of the duration of preoperative symptoms on the prognosis might be considered from three phases: (1) Its relation to the severity of the bladder infection; (2) the time elapsing before postoperative improvement, and (3) the postoperative mortality.

Although the severity of the bladder infection is largely dependent on the length of the preoperative symptoms there are other influential factors. It is not uncommon to observe marked inflammation and ulceration with symptoms of only a few weeks' duration. On the other hand a fairly normal bladder is occasionally found when the disease has evidently existed many months. Further, with occluded renal tuberculosis when the initial symptoms had occurred and ceased several years before, the cause of the bladder infection having been removed by autonephrectomy, the bladder usually became fairly normal.

In the majority of cases the duration of vesical symptoms persisting after operation diminished in direct proportion to the length of preoperative symptoms. Of the patients with preoperative symptoms of less than three or four months' duration improvement was noted immediately in 48 per cent. When the symptoms existed a year or more prior to operation immediate improvement was noted in only 15 per cent.

A review of the mortality records shows that there is surprisingly little difference in the mortality with regard to the length of preoperative symptoms of less than five years. It has been claimed that the mortality of patients with short duration of symptoms is considerably higher than that of patients of long duration, and that a relative degree of immunity is established among the latter. This, however, was not borne out in our cases, since the group of patients with symptoms of less than three months had practically the same mortality as the group in which the symptoms were of much longer duration. It is of interest that the mortality in the group of patients having symptoms more than five years is considerably less than the average. This is explained by the fact that many of these patients had either an occluded renal tuberculosis or a high degree of immunity. This group also included five patients who had no evidence of disease other than albuminuria and slight pyuria, and in whom the discovery of renal tuberculosis was largely accidental.

TABLE XI.—BILATERAL RENAL TUBERCULOSIS.

Patients with definite bilateral involvement	16
Patients reported dead (none alive longer than one and one-half years)	13
Patients living (less than two years after operation)	3

It has been claimed that in cases of bilateral renal tuberculosis if the more diseased kidney is removed the patient will often improve, and in certain instances recover. It has also been claimed that infection in the remaining kidney may be reduced or overcome by compensatory hypertrophy; this has not, however, been substantiated by the end-results in our series of bilateral cases. Thirteen of the 16 patients with proved bilateral renal tuberculosis are reported dead; 3 are living. None of the 13 patients lived more than

one and one-half years after operation, and all but 3 died in less than six months. The 3 living were operated on two years before their last report. One of these became steadily worse and recently had complicating perineal fistulas. The general health of the other two has temporarily improved. Both patients had a large, active tuberculous pyonephrosis on one side, which was removed, and a fair degree of function in the other kidney. Such patients improve because the toxemia of acute infection is removed, and not because of improvement in the other kidney. When an occluded caseated kidney was removed, little or no benefit followed. Unless one kidney is largely destroyed and the other is in fair condition, operation should not be considered; and then only when infection, pain, or possibly hemorrhage renders it imperative. Many cases of bilateral renal tuberculosis in which cure by operation was reported in the literature were probably not bilateral. Doubtless pus or tuberculous bacilli picked up by the ureteral catheter from an infected lower ureter while the kidney itself was normal could best explain such results.

TABLE XII.—MORTALITY.

Operations for unilateral renal tuberculosis	516
Operative mortality	7 (1.3 per cent.)
Patients with complete postoperative data	435
Deaths	105 (24.1 “
One year or less after operation	58 (55.2 “
Two years after operation	8
Three years after operation	6
Four years after operation	2
Five years after operation	7
Six years after operation	5
Seven years after operation	3
Eight years after operation	1
Nine years after operation	1
Ten years and over after operation	1
Date of deaths not given	13

The operative mortality (1.3 per cent.) is a comparatively negligible factor. The total mortality (excluding bilateral renal tuberculosis) is 24 per cent., which includes every death from any cause following operation, some occurring as long as ten or more years afterward.

Fifty-eight patients (55 per cent.) died within one year after operation. The relatively high mortality during the first year after operation has been previously noted by several observers. It would seem logical to regard the early death as an evidence of the virulence of the infection rather than as a result of the operation. It may be inferred that the probability of death from tuberculosis decreases inversely with the length of time after operation. Owing to the inability to get accurate data as to the cause of postoperative death, no attempt was made to investigate this factor.

Many patients died from diseases other than tuberculosis and from accidents, so that the late mortality from tuberculosis is really

much less than our figures indicate. Furthermore, a considerable proportion of the total number of deaths reported occurred more than five years after operation. It would be conservative and more accurate, therefore, to regard the actual late mortality as not more than 20 per cent.

One hundred and four (23 per cent.) of the living patients stated that they had not entirely recovered from their bladder symptoms. From many of these answers to inquiries were received in less than two years after operation, and it is safe to assume that at least 5 per cent. would eventually report recovery from their symptoms. Moreover, 64 patients reported a gain in weight and general condition, so that except for the bladder symptoms they were in a fairly good state of health.

It may be assumed, therefore, that approximately 80 per cent. of the patients will recover following operation for renal tuberculosis and that a complete cure, including cessation of urinary symptoms, may be expected in fully 60 per cent.

CONCLUSIONS.

1. Renal tuberculosis occurs most frequently between the ages of twenty and forty years (70 per cent.).

2. It occurs in the male almost twice as often as in the female.

3. The postoperative mortality in the male patient is somewhat higher than in the female.

4. The condition is usually not surgical in children; it occurs more often as a part of a general tuberculosis.

5. Evidence of tuberculosis in other tissues of the body may be found in fully 71 per cent. of the patients, if not in all.

6. The postoperative mortality among patients with coincident lesions is not higher than that of the general average.

7. Multiple lesions, unless they are a part of an acute general infection, do not necessarily render the prognosis more unfavorable.

8. Evidence of healed pulmonary tuberculosis is present in fully one-third of the patients.

9. The percentage of recovery among patients with healed pulmonary tuberculosis is above the average and may be considered indicative of increased powers of resistance.

10. Coincident active pulmonary tuberculosis was found in approximately 5 per cent. of the patients, of whom more than 60 per cent. recovered following nephrectomy.

11. Involvement of genitalia is present in at least 73 per cent. of male patients and does not seem to affect the ultimate recovery.

12. Frequency of spontaneous healing of lesions in the prostate and seminal vesicles contra-indicates their removal by subsequent operation.

13. Evidence of tuberculosis involving the bones and joints was noted in 6 per cent. of the cases; one-half of the lesions were active. The late mortality was 5 per cent., from which it may be inferred that the presence of such complications may be an index of increased resistance.

14. Spondylitis, usually healed, was present in 5.7 per cent., with a mortality of 12 per cent.

15. Chronic spondylitis does not influence the prognosis. Active spondylitis, although it does not contra-indicate nephrectomy, will not offer a favorable prognosis.

16. Tuberculous adenitis was present in 19 patients (6.4 per cent.) and the low mortality (10 per cent.) is suggestive of a heightened resistance.

17. Reduction in hemoglobin does not necessarily affect the prognosis.

18. The mortality among patients with marked bladder involvement is twice as great as with slight involvement. The degree of involvement is dependent not so much on the duration of symptoms as on the virulence of the infection.

19. The mortality percentage is markedly influenced by the degree of pathological involvement of the kidney, increasing in proportion to the extent of the lesion. Early lesions have the lowest mortality and pyonephrosis the highest.

20. Occluded renal tuberculosis is indicative of relative immunity and a low mortality.

21. The duration of preoperative symptoms does not materially affect the late mortality.

22. Recovery from bladder symptoms is more apt to occur, and earlier, when the preoperative symptoms are short than when they are long.

23. Recovery or permanent improvement of the remaining kidney will not follow after one kidney has been removed in cases of bilateral renal tuberculosis.

24. Operation in cases of bilateral renal tuberculosis is advisable only when there are acute unilateral complications, and then with no hope of eventual recovery.

25. Late mortality is much the highest during the first year; it decreases with the length of time elapsing after operation.

26. The operative mortality is a negligible factor; the late mortality (five years or less after operation) is approximately 20 per cent.; failure to effect complete cure is approximately 20 per cent.; this leaves a prognosis of recovery in 80 per cent. and of a complete cure to be expected in fully 60 per cent. of patients.

**DIAGNOSTIC SIGNIFICANCE OF THE FIRST SOUNDS OF
THE HEART.**

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CIRCULAR 21, S. G. O.,¹ issued especially to the cardiovascular examiners is a definite statement of the most advanced standpoint in the diagnosis of heart conditions, and as such deserves to be called to the attention of all clinicians.

One of the most striking features of Circular 21 is the absolute disregard of the systolic murmur, the interpretation of which is usually considered the ultimate test of our diagnostic ability. Lewis² had previously called attention to the lack of agreement among physicians as to the meaning of the various types of apical systolic murmurs. But neither Lewis, nor Janeway in Circular 21, offered a substitute standard for cardiac examinations.

Such a standard, I think, may be found by comparing the first sound over the right and left ventricles. Dana's³ recent confirmation of this idea leads me to believe that a statement as to the possibilities of this method would not be without interest.

The cause of the first sound of the heart seems to be an accepted physiological fact. At least the description varies little in the textbooks, and all agree in stating two factors, muscle contraction and auriculoventricular valve tension. As one studies the effects of mitral valve lesion on the first sound, one is led to doubt the usual explanation, at least, as applied to muscle contraction. If, however, one can consider the first sound as due to tension in muscle as well as in valve the changes in the first sound as a result of valve and muscle disease can be easily understood.

The theory of Martius, supported by Howell, that the first sound begins during the time of total closure of the ventricle, that is, when there is no movement of the blood within the chamber, seems to substantiate the idea that almost the entire first sound is a result of tension of both valve and muscle. It is true that the first sound lasts longer than the time of total closure, but it is also true that when there can be no total closure, that is, with mitral regurgitation, the first sound, making all allowance for the peculiarities of conduction, is absent. The laws of conduction of sound within the chest are but slightly understood, and for this reason the interpretation of sound heard must always be based upon changes in conduction as well as in character.

¹ Circular 21, Surgeon-General's Office, July, 1917.

² Medical Research Committee, Special Report No. 8, London, 1917.

³ Heart Muscle Equation, *AM. JOUR. MED. SC.*, June, 1919.

The evidence obtained by percussion in the examination of the heart is valuable in many instances, but in the very case where most needed a rigid thorax, an emphysema or some one of the other sources of error makes the result of percussion uncertain. When one has seen a clear-cut stereoscopic radiograph of the heart and mediastinum one is not inclined to rely very much upon the percussion outline.

So with systolic murmurs under suspicion as diagnostic criteria, and percussion outline unreliable, any procedure which will give definite information is to be utilized to the utmost. And such a source of information is to be found in the study of the first sounds of the heart.

Exactly the same series of events occur synchronously in the right and left heart, with the result that the normal heart sounds thus produced are fused into a single first sound; but just as we have been taught to differentiate systolic murmur by the point of maximum intensity and the direction of transmission, so we can learn to tell the first sound as created in the right heart from that in the left by studying these sounds at the point of optimum clearness. The sounds then can be compared by auscultation, first, over the right ventricle and then over the left. In the fourth or fifth interspace, just to the left of the sternum, the right first sound is heard most clearly, but considerable liberty of selection is allowed in order to find the place where there is the least possible interference from conduction. The first sound originating in the left ventricle is best heard just above and within the apex-beat, the classic area of mitral stenosis murmurs. How much depends upon the proper selection of these areas to avoid confusion can best be realized when one remembers the definite localization of the very loud presystolic murmur and snappy first sound of mitral stenosis.

In a normal heart the first sound right and left are practically the same in length and quality of tone, but the right not quite so loud.

The first sound over the right ventricle is almost always normal or standard, because disease of the tricuspid valve is rare, and such hypertrophy as occurs here is in total amount so slight that changes in sound due to this are beyond our interpretation.

Considering, then, the right first sound as the individual standard; comparing this with the left first sound as heard at the apex, we find that the left first sound may be increased, diminished, absent or show complete changes in character.

The increased first sound left is perhaps best typified by the booming first sound of aortic insufficiency. This seems to be due to increased muscle tension and varies directly with the amount of hypertrophy of the left ventricle and with the condition of the heart muscle. The first sound in infectious aortic insufficiency is louder and longer than in degenerative aortitis, in which there are usually

heart muscle changes as well. Hypertrophy of the left ventricle from any cause produces similar changes in tone quality of the first sound left, but when the hypertrophy is bilateral the tone quality of the right first sound is also affected, and then differentiation is more difficult.

According to Martius the first sound left must be absent in mitral insufficiency because this lesion makes it impossible for the left ventricle to have a "time of total closure."

In a very large proportion of the cases of pure mitral insufficiency we do not hear a first sound left, and it is perfectly safe to make a diagnosis of organic regurgitation, upon this combination of no first sound at the apex and a loud systolic murmur, with normal first sound right. Likewise, it is impossible to substantiate a diagnosis of mitral insufficiency when there is systolic murmur and a normal first sound left. Difficulty arises when a changed first sound left and murmur is heard, and in such instances a very careful examination is necessary to determine whether the first sound heard at the apex is conducted from the right side or whether, in truth, the first sound originates within the left ventricle. If the first sound has the same quality and tone as a normal first sound left, but is merely shorter in duration and followed by a murmur, the exercise test will many times cause the sound to disappear and be replaced, in its entirety, by a systolic murmur. Under these circumstances we have no hesitancy in diagnosing myocardial degeneration with relative mitral insufficiency. Even without the systolic murmur, shortening of the first sound left, with changes which seem to be due to lack of muscle tone, can frequently be changed by exercise into a definite systolic murmur without first sound; and here, again, we are justified in making a diagnosis of myocarditis with relative mitral insufficiency.

When the first sound as heard at the apex is shorter than the normal first sound on the right side, and of slightly different tone quality, the change not due to conduction and persisting through the exercise test, one must either dismiss entirely the diagnosis of mitral insufficiency or add thereto the diagnosis of mitral stenosis. The correct diagnosis can be made by a careful study of diastole in various postures and with different amounts of exercise, keeping well in mind the typical exercise response of mitral stenosis, which consist in suddenly developing dyspnea and peripheral cyanosis. Even when no murmurs can be heard in diastole this first sound may be an approach toward the snappy first sound of mitral stenosis, and must be considered as indicating possibly an early phase of mitral disease of the progressive type, which will ultimately develop a predominating stenosis.

The buttonhole mitral stenosis gives the most typical snappy first sound, which may be likened to the sound of a single stroke on the tambourine. For the purpose of comparison it may be said that

the valve element dominates this sound exactly as the muscle element dominates in booming first sound. Mitral stenosis can scarcely be diagnosed without the snappy first sound, but this, in addition to practically any form of diastolic murmur, save that of aortic insufficiency, means mitral stenosis.

In those cases of mitral stenosis presenting 3-4 rhythm, it must be remembered that the second of the sounds is the true first sound and is the one which has the characteristic tambourine quality.

When one has learned the difference in tone quality of the right and left first sound in a typical case of buttonhole mitral stenosis it is then much easier to pick out the changes described in the preceding paragraphs. It must be remembered that in double mitral lesions we cannot determine by auscultation which defect dominates in disturbing the physiology of the circulation. This important differentiation depends entirely on the size of the left ventricle, as shown by the position of the apex-beat and the percussion outline.

If we rely upon this classic combination of presystolic thrill, presystolic roll and snappy first sound, we will be able to diagnose only 30 to 40 per cent. of the cases of mitral stenosis. Any change in first sound left should direct our attention to a more careful survey of diastole, and we will then be able to recognize the early and atypical cases of mitral stenosis.

The first sound in Graves's disease is shortened both right and left and has a rather peculiar stroke, which allows one to differentiate it clearly from an equally rapid systole, due to other conditions. Usually in these rapid pulse cases the first sound right and left are similar, but in certain cases of neuro-circulatory-asthenia the right first sound remains normal while the left first sound takes on the quality of thyroid heart. It is interesting to note, however, that in those neuro-circulatory-asthenia cases which respond unfavorably to exercise from very slight exertion the right first sound also becomes quicker and shorter and approximates the left first sound.

In approaching death from infectious disease and also in so-called surgical shock cases there is a gradually increasing loss of tone in the first sound, both right and left, until twenty-four to thirty-six hours before death, we have the tick-tack heart in which the first and second sounds are alike, and from six to twelve hours before death one sound is lost, and upon the most careful auscultation only the single sound can be heard.

Incidentally, I may remark that after the stage of the tick-tack sound is reached I have never seen any form of stimulation bring about a reaction on the part of the heart muscle, although up to this stage, stimulation, preferably with the caffeine group, frequently brings about marked improvement.

Reduplication of the first sound is by no means infrequent, but as long as the reduplication occurs without disturbing the 2-4 rhythm of the heart no importance is to be attached to this. On

the contrary, when the extra sound changes the rhythm from 2-4 to 3-4 gallop rhythm it is always of the utmost significance. When we study this rhythm by comparison of the first sound right and first sound left, we find it almost always limited to the left ventricle, occasionally to the right, but exceptionally it may occur over both.

The synonym *rhythmus brightique* is given to this condition because it most frequently occurs in the left ventricle hypertrophied as a result of arteriosclerotic kidney, but it can occur in any form of hypertrophied heart muscle. The occurrence of the 3-4 rhythm localized over the right ventricle is not uncommon in kyphosis and other extreme deformities of the chest. This 3-4 rhythm always means degenerative hypertrophic heart muscle, which is on the verge of "failure" in Mackenzie's interpretation of this word.

Furthermore, demonstration of the 3-4 rhythm is a positive indication for the administration of digitalis which will usually restore the normal rhythm. If not treated with digitalis the case very soon progresses to the usual manifestations of conclusive decompensation. Since a very much larger percentage of cardiovascular-renal cases finally break under heart symptoms than is generally believed, eliciting this 3-4 rhythm as an early sign of approaching heart muscle weakness, is of great value.

Behavior of the first sound in the various forms of cardiac irregularity presents many interesting features. For instance, in mitral insufficiency of the type described above the long systolic murmur and no first sound, with ectopic beats, the first sound is heard over the apex with the premature contraction, and usually seems louder, the earlier and more incomplete the ectopic beat. This also holds true in cases of tricuspid insufficiency where the same condition can be demonstrated over the right ventricle.

In mitral stenosis with fibrillation the snappy first sound is heard only with those systoles which present a normal pulse wave, and inasmuch as fibrillation of the auricle does away with practically all diastolic murmurs a diagnosis of mitral stenosis again depends upon comparison of the first sound right and left.

I am quite aware that I have presented nothing new, and nothing that is not to be found, better described, in the text-books on physical diagnosis, but the fact remains that the teaching of physical diagnosis has always laid undue importance upon systolic murmurs in the study of the heart, and sounds have been neglected. Each clinician must learn for himself to interpret the phenomena of the heart, and in so doing he places more or less importance upon the sounds; but, unfortunately, he does not formulate this knowledge in such a way that it is available for demonstration, and what I have offered here is merely a suggestion to substitute for an illy defined memory picture of the first sound of the heart the normal standard of the right first sound.

REPORT OF DIABETIC SERVICE AT U. S. ARMY GENERAL HOSPITAL NO. 9, LAKEWOOD, NEW JERSEY.

BY FREDERICK M. ALLEN, M.D.,

AND

J. W. MITCHELL, M.D.

NEW YORK.

THE special diabetic service which was in operation in this hospital from the end of July, 1918, to the end of May, 1919, was the only one of the kind in the American army and was intended to receive all diabetic cases developing in the more easterly districts of this country or returning from overseas. Owing to imperfect notification and other obstacles, by no means all such cases were actually assembled here, so that the statistical value of this report is limited. Of the total number of 40 cases received, 3 proved to be so-called "renal glycosuria" and have been reported elsewhere.¹ Three others (Nos. 8, 16 and 37 below) have also been described separately^{2 3 4} because of certain special features. A summary of the observations concerning the entire 37 diabetic cases may be desirable as a record of military experience and for its instructiveness in some details.

ORGANIZATION OF SERVICE. An old hotel had been taken over for the hospital and it was necessary to improvise everything for the diabetic as for other services. The barber shop was transformed into a chemical laboratory and a bedroom and adjoining bath on the ward were made into a diet kitchen. With a suitable chemical staff and equipment, experienced nurses and the cordial support of the commandant and other authorities it was proved that accurate and effective treatment could thus be carried out.

STUDY OF CASES. The study was aided by the military requirement of a series of routine examinations and the coöperation of specialists in the various branches of medicine. The presence or absence of abnormalities was determined not only by general physical examination but also with the assistance of the eye, ear, nose and throat and dental, cardiac (including electrocardiographic), surgical, orthopedic, genito-urinary, radiographic, bacteriological and general laboratory services. The data obtainable have thus been increased in extent and value and the cordial helpfulness and absence of antagonism or intrigue also made this phase of the work a pleasure.

¹ Allen, Wishart and Smith: Three Cases of "Renal Glycosuria." *The Archives Int. Med.*, November 15, 1919.

² Mitchell: *AMER. JOUR. MED. SC.*, May, 1919, p. 700, vol. clvii, 5.

³ Allen and Mitchell: A Case of Hereditary Diabetes. Publication forthcoming.

⁴ Allen and Mitchell: A Case of Uncontrollable Diabetes. Publication forthcoming.

Physical examination.

Personal history.

Time elapsed.

Weight.

Age.	Race.	Civil occupation.	Family history.	Diseases.	Military service years.	From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.	Height.	Weight.			Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.	Wassermann
									Ordinary.	Admission.	Discharge.						
40	Amer.	Physician	Father and one brother diabetic and obese as a child	Mumps, measles and chicken-pox	1 1/2 not over seas	Few months	Immediately	6 ft. 4 in.	280	260	240	Negative	Negative	Negative	Negative	Neg.	
41	Amer.	Post office employe	Maternal grandfather died of diabetes	Mumps, measles and scarlatina as child	1 7/12 not over seas	Two months	Two weeks	5 ft. 10 in.	170	170	145	Negative	Negative	Negative	Knee-jerks diminished	Neg.	
55	Amer.	Newspaper reporter	No diabetes or obesity	Mumps in childhood	1 2/12 Shock and head injuries	Unknown	Unknown period of years	5 ft. 10 in.	210	180	145	False	Palpable posterior cervical	Liver palpable 2 cm. below costal margin	Knee-jerks increased	Blood sp. fl. ++	
37	Amer.	Metal minor	Maternal relatives obese	Mumps, measles, whooping-cough and scarlatina as child. Typhoid at 10 yrs. Malaria at 22 yrs.	3 5/12 not over seas	Two months	Immediately	5 ft. 10 in.	145	145	135	Negative	Negative	Palpable posterior cervical	Arteriosclerosis early	Negative	Neg.
34	Amer.	Physician	Father died of leucemia; 1 bro. of nephritis. No diabetes or obesity	Mumps, measles and chicken-pox in childhood	1 4/12 over seas	Intermittent	One month	5 ft. 8 in.	200	215	153	Negative	Negative	Scar of penetrating wound, left chest posterior	Negative	Neg.	
45	Eng.	Physician	No diabetes or obesity	Influenza, Sept. 18 over seas	1 3/12 over seas	One month	Three months	5 ft. 5 in.	145	137	126	Pyorrhea and caries	Negative	Negative	Negative	Neg.	
44	Amer.	Soldier	Familial obesity	Measles and whooping-cough as child. Malaria in 1889; tropical fever 1906; influenza, Oct. '18	22 not over seas	One month	Four months	5 ft. 11 in.	225	180	155	Negative	Negative	Heart enlarged to left. Liver palpable 5 cm. below costal margin	Knee-jerks absent. Romberg positive. Sensation impaired lower extremities	Blood neg. sp. fl. neg. p. g.	
43	Canada	Marine eng.	No diabetes or obesity	Mumps and phthisis in childhood	1 8/12 torpedoed	10 days	Immediately	5 ft. 9 in.	190	130	120	Negative	Negative	Inguinal adenopathy	Liver palpable 3 cm. above umbilicus. Maximum ascites; bilateral hydrothorax	Knee-jerks absent	Neg.

Glycosuria.	Symptoms.		Stay in hospital, months.	Maintenance diet.		Faithful to diet.	Other treatment.	Plasma sugar under treatment.	Prognosis and reason.	Remarks.	
	Acetonaemia.	Plasma sugar %		Plasma CO ₂ combining power vol. %	Protein.						Carbohydrate.
Heavy	Negative	0.356	2	100	125	3000	Yes	None	0.356-0.102	Good. Age and training.	Obese type.
Heavy	Heavy	0.400	2	70	60	1800	Fair	None	0.109-0.100	Fair. Age in patient's favor, but accidents are liable, as diabetes is not very seriously considered.	
Faint	Faint	0.250	3	70	40	2000	Fair	KI, mercury and salvarsan	0.25-0.09	Bad. Early paresis	Patient states that glycosuria went over a long period; could not get exact date of discovery.
Moderate	Moderate	0.200	1	70	50	1800	Yes	None	0.200-0.105	Good. Age and intelligence	
Faint	Moderate	0.129	3	70	100	2000	Yes	None	0.129-0.106	Good. Mild case; profession	Glucose tolerance (100 gm.) Dec. 1918. Urine, Urine. Plasma, Urine, Urine. sugar, % vol. c.c. sugar, c.c. fluid. I. 0.090 10 Neg. (fast) II. 0.250 75 3.38 III. 0.150 110 3.40 IV. 0.126 148 0.52
Heavy	Faint	0.48	3	None	could be prescribed	None	No	None	0.15-0.10	Bad. Lack of intelligence and persistent slight hyperglycemia	Glucose tolerance (50 gm.) Jan. 1919. Urine, Urine, Urine, Urine, Urine. sugar, % vol. c.c. sugar, c.c. fluid. I. 0.136 ... (fast) II. 0.250 38 0.50 III. 0.273 135 0.25 IV. 0.250 175 Negat V. 0.158 ... (fast) Obese type.
Heavy	Faint	0.356	3	80	80	2000	Yes	Physiotherapy	0.356-0.10	Good. Age, type and fidelity	
Heavy	Heavy	0.450	9	70	10	1500	No	Physiotherapy	0.400-0.12	Poor. Lactic cirrhosis and mental attitude	*Asotic fluid gave two plus Was Dec. 12, 1919. One week provocative dose of salvarsan (Wassermann was one plus; army culture).

Personal history.

Physical examination.

Rank.	Age	Race.	Civil occupation.	Family history.	Diseases.	Military service years.	From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.	Weight.	Discharge.	Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.
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Rank.	Age	Race.	Civil occupation.	Family history.	Diseases.	Military service years.	From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.	Weight.	Discharge.	Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.
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Rank.	Age	Race.	Civil occupation.	Family history.	Diseases.	Military service years.	From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.	Weight.	Discharge.	Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.
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2d Lt.	25	Amer.	Metallurgical engineering	No diabetes or obesity	Mumps, measles, scarlet and chicken-pox as child. Appendicitis. 1917, pus case	1 5/12 overseas	One month	Two months	5 ft. 6 in.	140	130	Negative	Negative	Negative	Negative	
Pvt.	23	Amer.	Clerk	One brother obese, no diabetes	Mumps and measles in childhood	11/12 not overseas	Two months	Immediately	5 ft. 6 in.	102	100	Negative	Cervical palpable	Depression of old skull fracture	Negative	
Pvt.	21	Amer.	Laborer	No diabetes or obesity	Denies all diseases	8/12 not overseas	Two months	Immediately	5 ft. 9 in.	138	130	Negative	Negative	Negative	Negative	
Corp.	23	Amer.	Teamster	No diabetes or obesity	Measles as child. Tonsillitis at onset of diabetes	5 3/12 overseas	Two months	One and one-half months	6 ft. 1 in.	188	130	Negative	General adenopathy	Negative	Knee-jerks diminished	
Cook	28	Amer.	Cook	No diabetes or obesity	Measles as child	11/12 not overseas	At once	Two and one-half months	5 ft. 10 in.	154	115	Negative	Negative	Negative	Rt. knee-jerk absent	
Sgt.	41	Amer.	Civil engineer	Father died following gall-bladder operation. No diabetes or obesity	Measles and scarlet fever as child. Fungus, influenza, Oct., 1915	1 not overseas	Three months	Six months	5 ft. 8 in.	175	152	Negative	Negative	Negative	Knee-jerks diminished	
Pvt.	22	Amer.	Cotton mill worker	Father died following gall-bladder operation. No diabetes or obesity	Measles, chicken-pox and smallpox as child. Rectal fistula in 1917, very chronic	7 1/2 overseas	Existed prior to military service, army discovered accidentally	Three months	5 ft. 11 in.	158	104	...	General adenopathy	Entire left lung and right lower dull with crepitant rales. Fluid in right chest	Knee-jerks absent	
Ex-Sgt.	32	Amer.	Clerk	No diabetes or obesity	Measles, mumps and diphtheria as child. Frequent tonsillitis. Chancre, 1908	7 not overseas	One month	Immediately	5 ft. 7 in.	130	100	95	Negative	Negative	Negative	Knee-jerks diminished
Pvt.	19	Amer.	Clerk	No diabetes or obesity	Measles and typhoid as child	11/12 not overseas	Six months	Immediately	5 ft. 8 in.	130	122	Negative	Cervical palpable	Negative	Knee-jerks diminished	
Pvt.	30	Dutch	Farmer	3 brothers tuberculous. No diabetes or obesity	Measles as child	5/12 not overseas	One month	Two months	5 ft. 8 in.	150	140	126	Negative	Negative	Negative	Negative
Pvt.	21	Amer.	Gunsmith	3 aunts tuberculous. No diabetes or obesity	Denies all diseases	2 not overseas	Five months	Immediately	5 ft. 11 in.	158	130	Negative	Negative	Negative	Negative	

Glycosuria.	Symptoms.		Maintenance diet.				Plasma sugar under treatment.	Prognosis and reasons.	Remarks.					
	Acetonaemia.	Plasma sugar $\frac{C}{100}$ mgm powder vol. $\frac{C}{100}$	Clinical.	Stay in hospital months.	Protein.	Carbohydrate.				Calories.	Other treatment.	Faithful to diet.		
Moderate	Negative	0.231	71.0	Polyuria; polydipsia; loss of weight and strength	3	75	100	2000	Yes	None	0.231-0.106	Fair. Intelligent, but youthful type		
Heavy	Moderate	0.204		Polyuria; polydipsia; polydipsia; blurred vision; loss of weight and strength	4	70	25	1200	No	None	0.220-0.406	Poor. Lack of intelligence and poor environment		
Heavy	Heavy	0.490		Polyuria; polydipsia; insomnia	6	70	25	1200	No	None	0.250-0.067	Poor. Ignorance and lack of will power.		
Heavy	Heavy	0.345		Tonsillitis; polyuria; polydipsia; polydipsia; pruritus; loss of weight and strength	5	70	80	2000	Fair	Tonsillectomy	0.500-0.064	Doubtful on account of environment		
Heavy	Heavy	0.278		Lassa-tide and furunculosis	3	60	10	1200	No	None	0.800-0.075	Bad. Ignorance and weak will	Died Feb. or March, 1919.	
Heavy	Heavy	0.378		Polyuria; polyphagia; polydipsia; loss of weight and strength	5	70	60	1800	No	None	0.378-0.086	Bad. Weak will and inherent severity of case		
Heavy	Heavy	0.800	23.0	Polyuria; polydipsia; polyphagia; weakness; loss of weight; cough; chest pain	5	70	50 to 0	1500-2000	No	Fresh air	0.800-0.425	Bad. Advanced tuberculosis and severe diabetes	Died May 9, 1919.	
Heavy	Heavy	0.600	76.7	Polyuria; polyphagia; polydipsia; loss of weight and strength	3	70	10	1200	No	None	0.25	Bad. Inherent severity of case and lack of will power	Blood Wassermann positive in negative 1911, two plus 1915 and five in 1917. Spinal puncture in 1915.	Died March 2, 1919.
Heavy	Heavy	0.470		Polyuria; polydipsia; polyphagia; lassitude; dizziness	4	70	50	1800	Yes	None	0.210-0.06	Good. Intelligent; good environment		
Heavy	Heavy			Polydipsia; polyuria	4	70	50	1800	Fair	None	0.178-0.077	Bad. Poor environment and ignorance		
Heavy	Heavy	0.400		Polyuria; polydipsia; loss of weight	4	70	80	2000	No	None	0.500-0.095	Bad. Untrustworthy		

Personal history.				Time elapsed.				Physical examination.						
Rank.	Age.	Civil occupation.	Family history.	Diseases.	Military service years.	From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.	Height.	Weight.	Tooth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.
						Admission.	Discharge.		(Ordinary)					
Corp.	30	Amer. Cement tractor	No diabetes or obesity	Measles chicken-pox and whooping cough as child Mumps measles-influenza in Dec., 17 and Oct., 18. Otitis media, bilateral, after onset of diabetes Tonsillitis at 21	7 1/2 overseas	Two months	Two months	5 ft. 8 in.	146 127 125	Negative	Chronic tonsillitis	Palpable cervical and inguinal nodes Negative	Negative	Knee-jerks diminished
Pvt.	20	Amer. Electrical engineering	Father died nephritis. Maternal uncle diabetic, obese type		1 overseas	One week	Immediately	5 ft. 10 in.	150 95	Negative	Chronic tonsillitis	Negative	Otitis media, bilateral	Knee-jerks diminished
Corp.	24	Polish Chain maker	No diabetes or obesity	Mumps and malaria as child. Respiratory infection preceding discovery of diabetes	1 1/2 overseas. Gas and shock 7 weeks not overseas	One month	Attempted at once; impossible in field hospital	5 ft. 11 in.	152 118 115	Negative	Chronic tonsillitis	Palpable cervical	Negative	Knee-jerks absent
Pvt.	22	Negro Farmer	No diabetes or obesity	Chills and fever every year	7 1/2 overseas	Two months	Immediately	5 ft. 5 in.	125 132 130	Carious, 2 assessed	Chronic tonsillitis	General adenopathy	Negative	Negative
Pvt.	28	Negro Laborer	Father, mother and only sister dead, cause unknown. Only brother tuberculous		7 1/2 overseas	Existed prior to military duty	Four months	6 ft. 1 in.	160 153 145	Carious	Negative	General adenopathy	Negative	Negative
Pvt.	24	Jew Printer	Mother died of diabetes. Consistent at 10 yrs.	Denies diseases of childhood. Never enjoyed good health, no stated reason	5/12 overseas	Two weeks	One and one-half months	5 ft. 10 in.	155 115 107	Carious	Chronic tonsillitis	Negative	Negative	Negative
Pvt.	25	Amer. Automobile	Father died of heart, condition diabetic. Both grandmothers died of either nephritis or diabetes	Mumps, measles and whooping cough as child	11 1/2 overseas	No symptoms	Two months	5 ft. 7 in.	129 137 114	Slight caries	Chronic tonsillitis	Negative	Negative	Negative

Symptoms.		Maintenance diet.				Stay in hospital months.	Clinical.	Other treatment.	Plasma sugar under treatment.	Prognosis and reasons.	Remarks.
		Plasma sugar %	CO ₂ in power vol. %	Carbohydrate.	Calories.						
Acetonuria		0.240	80	2200	4	Polyuria; polyphagia; polydipsia; loss of weight and strength	None	0.240-0.006	Good. Reliable and intelligent	Died Jan. 16, 1919, of acute streptococic meningitis secondary to otitis media. On day before death plasma sugar was 0.195 per cent. the CO ₂ combining power 63.3 vol. cent.
vy	Moderate	0.390	27.0	1	Polyuria; polyphagia; polydipsia; failure to gain weight following influenza	Ear irrigations and local applications	0.300-0.132	Poor. Infections present and severity of case	
vy	Heavy										
vy	Heavy	0.312	57.6	100	1900	3½	Polyuria; polyphagia; polydipsia; loss of weight and strength	None	0.440-0.097	Good. Intelligent and reliable	
vy	Slight	0.25	75	2000	3	Polyuria; polyphagia; polydipsia; weakness; pain in back	None	0.25-0.095	Bad. Ignorance and poor environment	Continuous acetonaemia due to bromine diet.
vy	Faint	0.606	75	2000	3	Polyuria; "tired feet," with loss of distal phalanges of all toes (gangrene?)	Mercury and salvarsan	0.606-0.110	Bad. Ignorance and poor environment	
vy	Heavy	0.313	70	1800	3	Polyuria; polyphagia; polydipsia; loss of weight and strength	None	0.454-0.122	Bad. Ignorance and untrustworthiness	An inherently mild case, but with continuous acetonaemia.
ative	Negative	0.125	70	1500	4	No symptoms	None	0.125-0.106	Poor. Ignorance	

Physical examination.

Personal history.

E. Age	Race	Civil occupation	Family history	Diseases	Military service year	Time elapsed		Weight		Discharge	Teeth	Tonsils	Lymph glands	Viscera	Nervous system	Wassermann
						From first diabetic symptoms to institution of the diet-therapy	From diagnosis to institution of diet-therapy	Height	Ordinary							
26	Amer.	Maedist	No diabetes or obesity	Measles and chicken-pox as child	17/12 overseas	One month	Two months	5 ft. 6 in.	135	97	98	Negative	Negative	Pendulous abdomen. Dullness at left apex	Negative	Neg.
27	Amer.	Food chemist	No diabetes or obesity	Mumps, measles and chicken-pox as child. Bone-monia at 15 yrs. jaundice in 1916, 1917 and 1918	11/12 overseas	One week	Immediately	5 ft. 5 in.	126	126	120	2 abscessed	Palpable posterior cervical	Slight epigastric tenderness. Spleen palpable	Negative	Neg.
27	Amer.	Chick	No diabetes or obesity	Measles and typhoid as child	7/12 overseas	Ten days	Immediately	6 ft.	150	146	131	Caries	Negative	Negative	Knees-jerks diminished	Neg.
36	Amer.	Steam fitter	No diabetes or obesity	Mumps, measles and chicken-pox as child	6/9/12 overseas	Five months	Immediately	5 ft. 8 in.	210	162	140	Crown and bridges, no abscesses	Negative	Negative	Knees-jerks diminished	Neg.
29	Amer.	Railroad brakeman	No diabetes, mother obese	Mumps and typhoid as child	11/12 overseas, Fractured 3 metatarsal bones	Two months	Immediately but high diets caused persistant glycosuria.	6 ft. 1 in.	185	150	140	Negative	Negative	Negative	Neuritis of 11th right intercostal nerve	Neg.
23	Amer.	Teamster	No diabetes or obesity	Mumps and pneumonia as child	6/12 not overseas	Two weeks	Immediately	5 ft. 10 in.	160	149	138	Negative	Negative	Negative	Negative	Neg.
27	Irish	Machine work	No diabetes or obesity	Mumps and measles as child	6/12 not overseas	One and one half months	Immediately	5 ft. 5 in.	140	112	110	Caries, 2 abscessed	Negative	Negative	Knees-jerks increased	Neg.
27	Amer.	Foundry work. No lead	Maternal family obese. No diabetes	Measles as child. Scarlet 6 weeks prior to admission	1 overseas	Four months	Immediately; treatment broken by lack of facilities on transport	5 ft. 10 in.	115	140	130	Negative	Negative	Palpable cervical	Negative	Neg.
28	Jew	Printer	No diabetes or obesity	Measles as child	6/12 not overseas	No symptoms; covered in routine examination	Immediately	5 ft. 5 in.	115	100	100	Negative	Negative	Negative	Negative	Neg.
26	Negro	Farmer	Father obese. No diabetes	Measles and malaria as child. Mumps Oct. 6, '18; Gonorrhoea 9 yrs. ago	10/12 not overseas	One month	Immediately	5 ft. 7 in.	112	137	130	Negative	Chronic tonsillitis	Palpable cervical and epitrochlear	Negative	Neg.
25	Greek	Cook's helper	No diabetes or obesity	Denies all diseases	11/12 not overseas or to military duty; discovered two months after induction	Existed prior to military duty; discovered two months after induction	Immediately	5 ft. 10 in.	140	110	...	Extensive caries and pyorrhea	Chronic tonsillitis	Negative	Knees-jerks diminished; no organic trouble found	Neg.

Symptoms.	Maintenance diet.				Pathful to diet.	Prognosis and reasons.	Remarks.
	Plasma sugar (C), comb. impower vol. C	Plasma (C).	Stay in hospital months.	Carbo-hydrate.			
Diabetes Mellitus							
Moderate	Negative	0.192	63.3				
Moderate	Negative	0.192	63.3	4	70	40	1500
Moderate	Faint	0.151		3	80	50	1100
Moderate	Negative	0.117		2	70	40	1800
Moderate	Heavy	0.375		4	80	40	1000
Moderate	Moderate	0.130		2½	80	40	1500
Moderate	Faint	0.221		2	80	20	1200
Moderate	Faint	0.15		3	80	40	1200
Moderate	Negative	0.210		1	80	40	1500
Moderate	Faint	0.147		1	80	40	1500
Moderate	Faint	0.297		1	80	40	1500
Moderate	Heavy	0.475	35.0	1			

X-ray corroborates physical findings in left apex.
 Patient failed to gain weight while valetising from acute interitis following treatment.
 Good, intelligent and trustworthy.
 Bad, ignorant and untrustworthy.
 Bad, ignorant and poor environment.
 Bad, ignorant and untrustworthy.
 Fair, ignorance may be overcome in institution.
 Fair, intelligence and fair environment.
 Poor, ignorance extreme.
 Fair, ignorance and racial characteristics.
 Bad, Extreme diabetes.
 Died May 17, 1919.

Glucose tolerance (100 gm).
 Plasma Urine, Urine
 sugar, C vol. o.o. sugar, C
 L. 0.115 (fasting)
 H. 0.250 16 0.45
 III. 0.326 76 0.70
 IV. 0.272 76 0.70
 V. 0.230 140 Neg.

Electrocardiogram shows sinus bradycardia. Eye-groundis suggest beginning retinitis.

DISCIPLINE. At first thought a military hospital might be regarded as an ideal place for enforcing rules of diet. Among soldier patients, however, are represented all the usual causes of recalcitrance, such as ignorance, weak will, recklessness, hopelessness of their condition and inclination to end everything as quickly and comfortably as possible by eating to satiety, not only the same as in civilian patients, but also to a greater degree, because a number are included who in civil life would never undertake treatment at all. In addition there are special motives, notably the fact that the patients had no choice, but were sent to take a treatment under compulsion, the grievances already nourished by some against the military service or officers, the habits of enlisted men in grumbling at the quantity and quality of their food, and the natural spirit of sport among them while leading the idle hospital life to see how far they could go in individual or organized disobedience without being detected or punished. Appeal to military law was inadvisable for several reasons: with patients as shrewd and well united as the average soldiers conviction is difficult; the sudden occurrence of glycosuria under fixed conditions is excellent proof of transgression for hospital purposes but not before a military court; pleas that they only ate when forced by extreme hunger would win sympathy and light punishment or none for the offenders; treatment in the guard-house was impossible unless with solitary confinement; and most important of all, the contention and hostility thus created between patients and officers would ruin the purposes of the service. Accordingly, no patient was subjected to any attempt at arrest or trial, but discipline was maintained by cultivating their knowledge and self-control. They were supplied with the best books and encouraged to find out anything they could through independent reading and inquiries in order to convince them of the seriousness of diabetes and the necessity of dietetic treatment; and at first they were allowed full liberty of movement. When they unanimously and flagrantly broke diet they were confined first to the ward and later to their rooms, not by military guards but by attendants, as in a civilian hospital. Against stealthier violations of diet with protein and fat, substitutions of urine and other familiar tricks, the rule was maintained that blood as well as urine must be constantly normal. Fortunately the first patients had not the severest diabetes, and it was possible to prove to them in confinement that they could be free from hyperglycemia and acidosis on satisfying and appetizing diets. By having the blood-sugar taken at unexpected times they quickly learned that this was a test which they could not cheat or evade. Essentially through the fact that the blood-sugar level decided between food and freedom on the one hand and fasting and confinement on the other, the initial spirit of rebellion died out in about two weeks so completely that it never revived. Thereafter only sporadic individual lapses had to be dealt with, and the general

fidelity was able to meet the two crucial tests of the *esprit du corps* of a diabetic department. One of these is that every patient, without exception, at discharge had feelings of gratitude and the determination (varying with his strength of will) to continue his diet and remain sugar-free outside the hospital. The other is that the patients in the hospital were mutually helpful; the newcomers acquired from the older ones confidence, obedience and knowledge of food values, so that a minimum of instruction or discipline was necessary.

ETIOLOGY. The possible causative influences may be considered under the following headings:

HEREDITY. The record of six patients with diabetic relatives out of a total of thirty-seven is probably higher than would be generally found in an equal number of non-diabetic cases and tends to confirm the existence of a hereditary element, especially if it be conceded that some instances were probably missed on account of the ignorance of many of the patients concerning their family history. The family incidence of obesity, tuberculosis and neoplasms is probably rather high, though exact reckoning is unprofitable for the above reason. The remarkable hereditary features of Case No. 15 furnished the subject of one of the special papers referred to previously.³

RACE. The proportion of two Jews and three Negroes was unusual. More of the former and fewer of the latter would naturally have been expected. The relation may have been accidental and the statistics for the entire army may be very different. Otherwise nothing special was noticed in the racial incidence.

CHARACTER AND CONSTITUTION. Patient No. 37 was mentally inferior.⁴ The others were fully up to the average of soldiers mentally and physically, and, on the whole, were of an excellent type in both respects. The experience tends to discredit the idea of general constitutional defects in diabetics.

DIET. Neither excess in carbohydrate nor general gluttony was apparently more prominent in these patients than among the average population, and there was no evidence of diet as a primary cause in any case. If patient No. 1 had eaten less the development of his diabetes would presumably have been delayed or perhaps prevented, according to the known rules of treatment, and the same may be true of the others in proportion to their obesity and habits. In the majority of the series overeating was not evident even as an exciting cause, and the proportion of thin and abstemious patients equalled or exceeded that of fat and gluttonous patients. In general, such observations will perhaps hold more strongly for young persons than for the more elderly type of diabetics.

NERVOUS CAUSES. No soldier in this series was markedly neurotic and the great majority were strong and well poised, sometimes phlegmatic. The high proportion of nine officers to twenty-eight

enlisted men is probably artificial, because the urine of officers was examined more often, and they were more likely to come for special treatment. Thus, one of the officers was not from the army but from the navy, and some of the others had made special efforts to be transferred to Lakewood. The greatest advantage of such a service in regard to the theory of the subject lay in the opportunity of observing possible cases of diabetes following physical or psychic shock, strain or injury. Only one case was encountered in which the onset of glycosuria seemed, with considerable probability, to date from a tremendous shock, and this proved to be renal glycosuria. Patient No. 22 was gassed with mustard and chlorine and a few hours later suffered concussion from a high-explosive shell. He was sent to a field hospital on account of "nervousness and excitement" and thence to a rest camp, in which clinical symptoms of diabetes were noticeable for the first time and the diagnosis was made by urinalysis a few weeks later. The most probable assumption is that a diabetic predisposition existed in such a case, and the lack of prior urinalyses prevents decision whether the shock came before or after the beginning of the glycosuria and concerning its role in the causation. Two other patients had histories somewhat like this one. No. 8, the naval officer, was on a torpedoed vessel and suffered from anxiety and exposure, though not wounded. No. 3, a captain of artillery, sustained head injuries in a motorcycle collision at the front, and a month later was blown up by the explosion of an ammunition dump from which he was trying to rescue a wounded comrade. Glycosuria and other diabetic symptoms followed in each case, but it happens that in each of these the existence of diabetes was known before the injury. Even an aggravating influence of the shock is not established, for in the former instance the improper diet on reaching port sufficiently explained the outbreak of symptoms, and in the latter case the diabetes remained mild, as it had been before. Wounded or sick soldiers were the ones most often subjected to urinalysis, and it was therefore natural that the diagnosis should often be made at such a time. Thus, patient No. 31 fractured three metatarsal bones during debarkation in France, and diabetic symptoms and glycosuria were noticed shortly thereafter. On the other hand the rarity of glycosuria after injuries is the striking lesson of the war. Also a large number of glucose tolerance tests performed by various medical officers for various purposes upon men returning from overseas suffering or convalescent from medical or surgical conditions have shown no special diabetic tendencies. If such tendencies were created in any marked degree by any form of injury, shock, strain or suffering, it must inevitably have been revealed by the observations on a wholesale scale in the different armies and even the civil populations. The war has been in this respect an immense experiment on human beings, establishing firmly some conclusions which could scarcely have been settled by

animal experimentation. While nervous influences are not excluded as affecting diabetes when the disease or predisposition is present, the main contribution of the war to this subject is the fact that the epidemic of diabetes which was to be expected on the nervous hypothesis of the etiology did not occur, and consequently this hypothesis, as concerns the primary cause of the disease, is decisively overthrown.

SYPHILIS. This infection was demonstrated in 4 of the 37 cases. Patient No. 3 had a definite history, strongly positive Wassermann reactions in blood and spinal fluid and early paresis. No. 8 had first a negative Wassermann in the blood, later a one plus after a provocative dose of salvarsan, a two plus (army nomenclature) in the ascitic fluid and a cirrhosis of the liver which responded markedly to specific treatment. No. 16 had a history of a chancre in 1908 and double plus Wassermann tests in the blood in that year and 1915. His diabetes was discovered following circumcision in 1915 and progressed downward notwithstanding military treatment, which made his blood Wassermann negative, the test being also found negative in the spinal fluid. No. 23, a Negro, had a history only of gonorrhoea and no symptoms or signs except a two-plus Wassermann reaction. No. 22 was reported to have a one-plus blood test, but the negative findings in all other respects were accepted as excluding syphilis. Careful examinations gave no grounds for suspicion in the other 32 cases.

OTHER INFECTIONS. Matters as trivial as an occasional small cavity in a tooth are omitted from the table. The dental service found small root abscesses in 6 cases. The extremely bad teeth of patient No. 37 may have had etiological importance.⁴ The 17 cases of chronic tonsillitis tabulated are mostly technical diagnoses, which did not cause the throat department to advise tonsillectomy and can scarcely serve to incriminate the tonsils. The personal histories of the patients, as a whole, included about the usual list of miscellaneous infections. In 7 cases suspicious events antedating the diabetes were elicited as follows: No. 7 had malaria and "tropical liver" in 1906, and the liver is still enlarged; diabetes was discovered in September, 1918, and became worse with influenza the following month. No. 9 had appendicitis with peritonitis and operation in April, 1917, passed examination (with urinalysis) for commission in November, and the first symptoms and diagnosis of diabetes occurred in May, 1918. No. 12 contracted acute tonsillitis at the front in May, 1918, and diabetes followed immediately. No. 14 had "grippe" in October, 1917, followed immediately by diabetic symptoms. No. 21 had influenza and pneumonia, followed immediately by diabetic symptoms. No. 23 (Negro) likewise had a respiratory infection, returned to duty after two weeks, felt weak and after seven weeks was forced to enter the hospital, where diabetes was diagnosed. No. 28 had pneumonia at fifteen and several attacks of

jaundice since. In October, 1918, he inhaled a little mustard gas and immediately developed jaundice, clay-colored stools and tenderness in the gall-bladder region, followed within two weeks by diabetes. Such histories are very suggestive, especially in view of their number; but the same care must be used as in the judgment of trauma and shock, and these cases can never be fully conclusive for the same reasons. In several cases of this series, dental caries and pyorrhea, boils, influenza and other infections are known to have followed the onset of diabetes, in conformity with the familiar lowering of resistance in this disease; and in case No. 34 the history of scarlet fever six weeks before admission seemed significant until it was found that the diabetes was of four months' duration. Also the above-mentioned fact that the sick most often have their urine examined, and the aggravation of an existing diabetes which is known to result from infection may likewise serve to explain the observations of both glycosuria and other symptoms under these conditions. The decision is governed chiefly by pathological evidence⁵ that the origin of diabetes is regularly in an infectious pancreatitis. Infections of the above character thus acquire significance as the causes of such pancreatitis, and also syphilis, which is known to cause pancreatitis, is easily understood as a cause of diabetes in certain cases. The combination of the above 7 cases and the 4 hetic cases makes a high proportion of cases in which the infectious origin is directly suggested. It so happened that in Case No. 21 the assumed pancreatitis could be verified by autopsy, and the same pathological basis was also found in the two other cases which came to autopsy. It may therefore be concluded that the origin of military and civil diabetes is the same.

TYPE OF CASES. There was some expectation that soldiers would furnish a selected group of cases of recent onset in young persons. The severe type characteristic of the young did in fact predominate, but the chance to treat such cases in their earliest and most hopeful stage was seldom obtained. Some diabetics were accepted in the draft and in others the diagnosis and treatment were delayed surprisingly long, as shown in columns 9 and 10 of the table. On the whole the cases were about the same as an average group at similar ages in civil life. Stated otherwise, this means that doctors overlook diabetes to about the same extent in military and in civil practice, and that in general the lack of early diagnosis is the greatest obstacle to the attainment of the best therapeutic results.

TREATMENT. All discoverable abnormalities were treated as in normal persons; carious teeth were filled or extracted; arsphenamin, mercury and iodides were used in the hetic cases and tonsillectomy was performed in case No. 12, which began with tonsillitis. As usual a probable cause of downward progress was thus removed, but

⁵ Rockefeller Institute monograph No. 11, 1919, Chapter VIII.

in no instance did the diabetes run a course different from the average thereafter. As permanent damage has generally been done in the pancreas it is unreasonable to expect a cure of diabetes by removal of the infectious cause. The diabetes was treated by initial fasting until glycosuria ceased, followed by a diet of protein and generally a little carbohydrate until hyperglycemia and acidosis were abolished. The diet was then built up, especially with fat, as shown under "maintenance diet" in the table, the allowance of all three classes of foods being governed by the severity of the case and normal blood-sugar and negative nitroprusside reactions being insisted upon throughout.

RESULTS. Mention should first be made of the 5 deaths, 3 in hospital and 2 outside. Patient No. 15 had advanced tuberculosis and acidosis at admission, improved temporarily and died after five months.³ No. 21 entered with a middle-ear abscess and died of meningitis before the diabetes was thoroughly under control. No. 37 was an extraordinary case in which the diabetes could not be controlled by fasting.⁴ Patient No. 13 was a hopelessly weak-willed individual who improved during three months in hospital but required confinement most of the time; he was discharged into bad environment, made a brief attempt to continue diet, then ate at will and died within three months. No. 17 had inherently very severe diabetes, but in conduct was one of the best in the series; after four and one-half months in hospital, during which he was in excellent condition, he was discharged with a good prognosis and died within two months. The danger lay in allowing such a patient to live far away from the supervision of any specialist. The terminal symptoms of nausea and collapse suggest fasting acidosis, and the boy possibly overstepped his diet unintentionally and encountered disaster when he tried to check symptoms by fasting.

RESULTS CONCERNING COMPLICATIONS. The fatal ending of tuberculosis and middle-ear abscess was mentioned above. Otherwise complications have ended favorably or failed to develop. Tonsillectomy was safely borne and every patient has responded to dental or surgical treatment like a normal person. During the extensive influenza epidemic it so happened that no diabetic patient acquired it, though they were equally exposed with other patients. The freedom from the traditional tormenting complications of diabetes is one of the principal benefits of thorough treatment, and the higher resistance to infection of the patient kept symptom-free by undernutrition as compared with the one who has active diabetes is a point to be emphasized.

RESULTS CONCERNING DIABETES. With the exceptions mentioned it was possible to attain freedom from hyperglycemia and acidosis in all cases and to maintain this freedom on a diet supporting the body weight at a level inversely proportional to the severity of the case. The few cases in which the table shows a "mainte-

nance diet" of only 1000 to 1200 calories were some in which diet had been broken so that treatment was not complete at discharge, though they were not more severe than some others. It is recognized that in cases more severe than these the standard of treatment mentioned sometimes necessitates extreme emaciation and weakness if the attempt is to be made to prevent downward progress by keeping the diet strictly within the assimilative power. These distressing end-stages may be either prevented or postponed by application of the same principle in the earlier stages, and for this purpose it will be noted that the diet in even the mildest cases was fixed so as to maintain a reduced level of weight.

PROGNOSIS. Notwithstanding the general favorable progress in hospital the prognosis is recorded as unfavorable in a high proportion of the cases. It unfortunately is still unproved whether the best treatment by the present methods can succeed permanently in arresting the downward progress in severe cases. But when poorly educated patients must go out to make their living in unfavorable environment without proper supervision, the result can be easily foretold. Unsuccessful attempts were made to interest the Red Cross and other organizations in establishing some institution or colony for the after-care of such patients, whose fate is typical of the neglect of chronic disease among the poorer classes in most communities.

STUDIES IN BONE GROWTH: AN EXPERIMENTAL ATTEMPT TO PRODUCE PSEUDARTHROSIS.

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ASSISTED BY

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THE studies herewith presented, and others which will be published later, were made possible through the generosity of the Surgeon-General in permitting the addition of a well equipped animal research annex to the pathological laboratories at U. S. Army General Hospital No. 3, Colonia, N. J., thereby affording facilities for the continuation of investigations relative to bone growth and allied subjects.

In the early months of our participation in the War, during the preliminary organization of this hospital under the joint auspices of the Red Cross and the Surgeon-General's Office, the author, who had been designated as director of the hospital, was allowed to draw

the plans of the laboratories to include not only the usual pathological and bacteriological departments, but a completely equipped animal research annex. As a result of a conference with Colonel F. F. Russell, M.C., Chief of the division of laboratories, privileges were granted which anticipated the work included in this paper by making ample provisions for further research in bone metabolism.

U. S. Army General Hospital No. 3 was opened for the treatment of surgical cases in the summer of 1918, the first patients being admitted early in July, 1918. En passant, it is of interest to note that of all the hospital units whose preliminary organization was made under the Red Cross, in conjunction with the Surgeon-General, this institution was the only one to be ultimately established as a military hospital in this country.

The laboratory, as planned at U. S. Army General Hospital No. 3, included animal houses, animal operating-room and animal autopsy-room, as well as the usual departments of the clinical sections of the laboratory, namely, large chemical, bacteriological and pathological rooms. Coincidentally with our clinical bone work, research in various allied problems was made since the early days of the hospital's establishment. These experimental studies were carried on under the auspices of the Surgical Service, with the close and efficient coöperation of the laboratory staff.

Such resources in equipment and technical assistance permitted the continuation of investigations especially desired by the author; foremost among which were an experimental study of the etiology of pseudarthrosis and an attempt to discover some trustworthy artificial stimulus to osteogenesis. This research was carried on with the object of supplementing earlier investigations,¹ made about ten years ago at the Cornell Animal Hospital, which dealt with various phases of bone growth, such as the experimental fusing of dogs' vertebrae by means of the inlay graft, and studies of the relative osteogenesis of bone obtained from various portions of dogs' and rabbits' anatomy. It was found at that time that cubes of bone removed from the spinous process of a vertebra were much less active osteogenetically when placed in a muscle belly, than were cubes of the same size taken from the shaft of a dog's long bone, thus proving the advisability of employing the bone graft for fusing the vertebrae in such conditions as caries of the spine, compression fractures of the vertebral bodies, selected cases of scoliosis, et cetera.²

Other experimental investigations were made at that time concerning the relative osteogenetic properties of the periosteum when

¹ Albee, F. H.: An Experimental Study of Bone Growth and the Spinal Transplant, *Jour. Am. Med. Assn.*, 1913, lx, 1044-1049.

² The lowered osteogenetic potency of the spinous processes of the vertebrae, largely due to their meagre periosteum and excess of ligamentous attachments, was clearly demonstrated by these experiments. Therefore, in attempting fusion of the vertebrae, it is more trustworthy to inlay a bone graft which thus supplies the needed osteogenetic activity at the same time that internal fixation is produced.

secured by *scraping the outer surface of the bone* with a sharp instrument, as compared with the osteogenetic power of the outer portion of the periosteum when obtained by means of *separation through the easier line of cleavage* with the use of a blunt instrument. In the first instance, the *complete* periosteum was obtained, and this was found to be a very potent osteogenetic element, whereas, in the latter case, osteogenetic activity was found to be only localized in those spots where portions of the cambium layer (which, alone, contains the active bone-growing cells) happened to come away with the so-called "limiting membrane" of Macewen. Studies were also continued which bore out the inadvisability of attempting the transplantation of bone tissue from one species to another, such as the grafting of sheep's bone into a dog, or dog's tissue into a rabbit. These latter findings, it is believed, bear very materially upon the ruling out of any attempts to transplant animal bone into the human subject and the advisability of always using, when possible, autogenous graft material.

Our bone research work at U. S. Army General Hospital No. 3 included an experimental study of pseudarthrosis, with a special object of determining the influence, if any, exerted by the roentgen ray upon callus formation. Another purpose of our investigations was to discover some trustworthy artificial stimulus to osteogenesis. A report of these latter findings will be published by the author at an early date.

The first experimentations at this hospital were carried on in an endeavor to ascertain, if possible, the etiological factor in pseudarthrosis, or malunion. One has but to observe the vast amount of literature written on the subject to realize the surgical importance of this condition. Whether the ever widening interest in this unfortunate malady is indicative of an actual increase in its prevalence, under our modern methods of living, is open to debate. The experience of the author, during the past fifteen years, would certainly bear out the impression that pseudarthrosis is on the increase. This conclusion has been strengthened by discussion with many colleagues likewise interested in bone work. In this connection, a Canadian surgeon recently assured the author that, in his opinion, change of diet necessitated by the Great War was the cause of the very large increase in such cases in his own practice. Among the many factors³ to which has been attributed a possible role in the causation of pseudarthrosis, special attention has been given to the following:

1. *Method of Splinting.* A consideration of influences possibly favoring the production of pseudarthrosis has included the type of splint and its adjustment in relation to interference with normal circulation; the length of time that the splint should be worn; the proper time for instituting massage; the type of coaptation splints; and the value of traction.

³ In passing wholly from clinical experience, it is the opinion of the author that syphilis has been greatly overestimated as a cause of this condition.

2. *Diet.* As referred to above, diet has frequently been discussed as a possible cause, in its relation to sluggish bone growth.

3. *Location of the nutrient artery,* with respect to the fracture, and the possible interference therefrom with the blood supply to the region of the fracture.

4. *Presence of Systemic Disease.* Lues, or atrophic conditions, such as neuro-arthropathies, etc., have been considered, in their influence upon bone metabolism.

5. *The Internal Application of the Metal Plate.* From the author's clinical experience, this would appear to be one of the most frequent causes of pseudarthrosis. In this hospital, there have been a goodly number of cases of malunion, without loss of bone substance, all of which have occurred in young soldiers, averaging unusual good health. In a large percentage of these cases, metal plates had been previously applied.

6. *The Roentgen Ray.* It is an established fact that repeated massive exposure to the roentgen ray is a potent inhibitor to cellular growth, in reference to spermatozoa, etc.

Of all the influences enumerated above, that of the roentgen ray is the only one which has been markedly increased within the last decade. In a modern bone clinic, it is, indeed, a rare exception when a fracture is not subjected many times to radiographic examination. The remarkable increase in prevalence of pseudarthrosis coincident with the coming into common usage of the roentgen ray presents a possible correlation. In a consideration of factors contributing to the causation of pseudarthrosis, it seemed, therefore, to the author that the influence of the roentgen ray should be one of the first to be investigated.

In our studies in bone growth, rabbits were selected as the experimental subjects. Young to middle-aged adults were chosen, no animals of either age-extreme being used. Careful asepsis was invariably observed, the field of operation being always treated with a $3\frac{1}{2}$ per cent. tr. iodine preparation. In our entire series of cases, numbering over 80, together with controls, there were but 2 instances of infection. These both occurred in the earlier studies in pseudarthrosis, and were in cases of compound fracture of both bones of the foreleg.

In the majority of our early experiments, it was our method to fracture both bones of the foreleg, an external splint being then applied for fixation and support. The numerous contrivances which are employed for such purposes vary widely in efficacy and cost.⁴

⁴ While studying methods of rehabilitation in Canada, the author was especially impressed with one type of splint that was shown him at a certain institution. It was a rather complicated, hinged device, of aluminum, consisting of several parts riveted together, and was manufactured at that hospital in a shop specially organized for the purpose.

The contrast, in cost of material and of manufacture, between this splint and one about to be described is worthy of consideration.

In an attempt to secure an adequate splint for the rabbit's leg, one that would at once maintain immobilization of the fractured fragments, as well as prevent the animal from gnawing its foot, the following extremely simple method was devised of producing an efficient splint:

A piece of copper wire mosquito-netting, 3" x 6", is placed on a pine board with the center of the netting square directly over a hole, $\frac{5}{8}$ inch in diameter, through which by means of a blunt soft pine plug, the netting is driven by a mallet and moulded into a cylinder, one end of which is closed. By trimming with the shears, the desired length is secured.

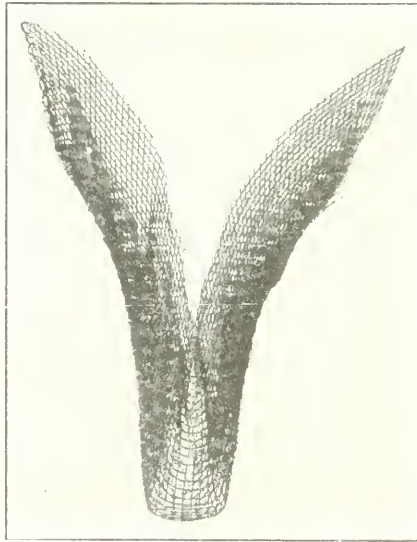


FIG. 1.—Splint for rabbit's leg—a simple and efficient device for maintaining immobilization of the fractured fragments, and one which will prevent the animal from gnawing its limb. This splint is made of copper wire mosquito-netting in the manner shown in Fig. 2. It is trimmed to the desired length and held in place by means of narrow strips of adhesive plaster.

After painting the line of sutures with 3½ per cent. tr. iodine and application of the proper gauze dressing to the compound fracture, it was an easy matter to draw this *combination boot and splint* over the animal's leg and to fasten it with narrow strips of adhesive plaster (Fig. 1). Animals splinted in this manner were less able to injure their limbs or interfere with the progress of the experiment. The extreme simplicity of manufacture of such a device (as shown in Fig. 2), together with its minimal cost,⁵ seemed to the author additional factors favoring its use.

⁵ Computed at the present wartime price of copper-wire mosquito-netting, at 12 cents per square foot, the actual cost of these rabbit splints is a cent and one-half apiece.

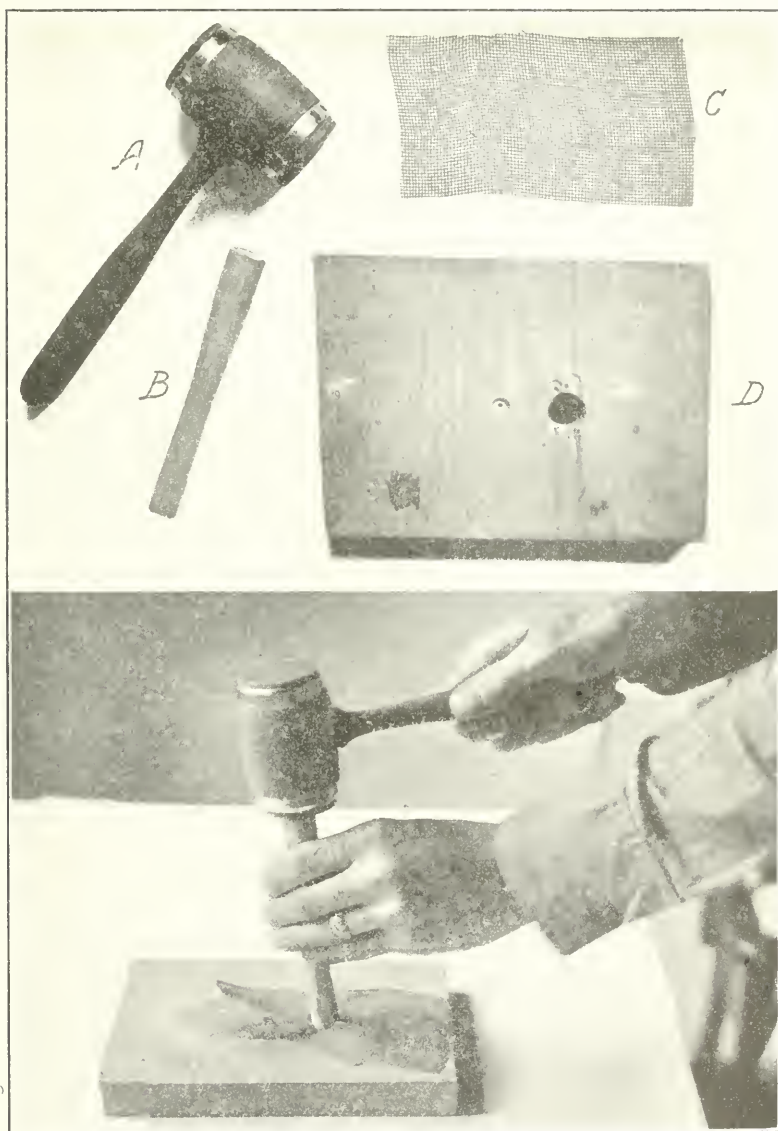


FIG. 2.—In the upper picture are shown the only materials required in the manufacture of the rabbit splint, illustrated in Fig. 1. These consist of a mallet, *A*; blunt soft pine plug, *B*; piece of copper wire mosquito-netting 3" x 6", *C*; and a pine board, *D*, which contains a hole $\frac{3}{8}$ inch in diameter. The copper wire mosquito-netting is placed on the pine board, with its center directly over the hole. Through the hole, by means of the blunt plug, the netting is driven with a mallet and moulded into a cylinder, in the manner demonstrated in the lower photograph. The cost of these extremely simple, but efficient splints, is exactly a cent and one-half apiece.

In the later portion of our series of experiments relative to the etiology of pseudarthrosis, it was found possible to fracture, by open operation, only one of the two bones of the foreleg, the other bone serving as a splint. External splinting was, thereby, avoided. In these cases, it was our method, after careful approximation of the skin edges by interrupted linen sutures, to paint the line of suture well with $3\frac{1}{2}$ per cent. tr. iodine, and to return the rabbit to its cage, without dressing or splint. Animals treated in this manner cared for themselves very well, and it was found that the wound healed quite as rapidly and without the occurrence of infection.

Our first animal experimentations at this hospital, numbering nearly a score, are included in this paper. These studies dealt with the roentgen ray, the removal of various amounts of bone and methods of splinting as possible causes of pseudarthrosis. Detailed reports of these experiments have been omitted, since, in every instance, the same result was obtained, namely, prompt union of the fractured fragments, usually with ample callus formation. Briefly summarized, our investigations and results were as follows:

(a) In one series of cases, sections of bone were removed from the radius, leaving a hiatus of considerable size, care being taken to remove *all* the small bone fragments. In every instance, prompt union by ample callus formation occurred.

(b) A second series of the same type of case as the foregoing, was then subjected to repeated long exposures to the roentgen ray; these cases likewise promptly united.

(c) A series of the same type was also splinted, as adequately as possible (see Fig. 1), and in other cases, no splint whatsoever was applied, the other bone of the foreleg being relied upon for support and to secure general alignment. Union in every case occurred promptly.

(d) In another series of cases, bone fragments were allowed to remain in the hiatus; as was anticipated, these cases showed a much more rapid bone growth than did those in which all the fragments were removed. Union occurred promptly, whether splinted or not, and whether or not subjected to massive and frequent exposures to the roentgen ray. Attention should be drawn to the clinical value of these observations which demonstrate the advantage of leaving *in situ*, whenever possible, attached fragments of bone in comminuted fracture, rather than removing them, as is frequently done by surgeons who do not grasp the fundamental laws of bone growth.

Following the suggested role of the roentgen ray as a possible factor in the etiology of pseudarthrosis, an experimental test of such a possibility was made on a series of cases. In each instance, after removal of $\frac{1}{4}$ inch of bone from the shaft of the right radius, the rabbit was subjected to massive roentgen-ray exposures at intervals of about five days, 5-inch gap, $3\frac{1}{2}$ ampères, being used for five minutes. As controls, the left radii of the same animals were later treated in

like manner, but without massive exposures to the roentgen ray. In the two groups of cases, no appreciable difference was found in the length of time required for union of the bones.

Illustrative of our attempts to produce pseudarthrosis by massive exposures to the roentgen ray, is Case No. 8, which, together with its control, is reported in detail, as follows:

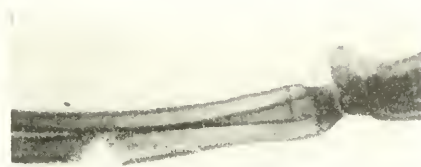


FIG. 3.—Case No. 8.—Second day after operation, showing gap in right radius from removal of $\frac{1}{4}$ inch of bone. This case was subjected to massive roentgen-ray exposures, 5-inch gap $3\frac{1}{2}$ ampères being used for five minutes. This treatment was begun on the day after operation and continued for 4 successive intervals of about five days.

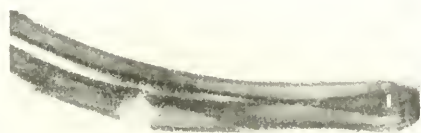


FIG. 4.—Case No. 8.—Twenty-five days after operation, showing evidence of a slight degree of bone growth. This radiograph was taken five days after the last of the series of massive roentgen-ray treatments.

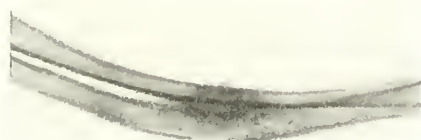


FIG. 5.—Case No. 8.—Forty-three days after operation, and about three weeks (twenty-three days) since last massive roentgen-ray treatment. Union is complete. Note that this radiograph shows more active bone growth and a more complete union than its control on which the roentgen ray was not used, save for short exposures in order to note progress of union.

CASE No. 8.—Subject, common hare.

March 20, 1919. Fragment of bone, one-quarter inch in length, removed from shaft of right radius.

Exposures to roentgen ray.

March 21. Subjected to 5-inch gap, $3\frac{1}{2}$ ampères, for five minutes.

March 25. Above treatment repeated.

March 30. Above treatment repeated.

April 1. Above treatment repeated.

April 9. Above treatment repeated.

Radiographic findings:

March 22. Second day after operation, roentgen ray shows gap of $\frac{1}{4}$ inch in shaft of radius. (See Fig. 3.)

April 14. Twenty-five days after operation. There is evidence of a slight degree of bone growth. (See Fig. 4.)

May 2. Forty-three days after operation—complete union is shown. (See Fig. 5.)

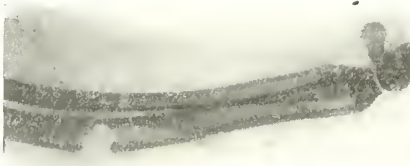


FIG. 6.—Case No. 8a.—Control of Case No. 8. Second day after operation showing $\frac{1}{4}$ inch gap in left radius. This case was not subjected to massive roentgen-ray exposures.

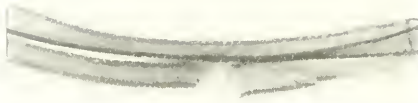


FIG. 7.—Case No. 8a.—Twenty-five days after operation. There is some evidence of bone proliferation.



FIG. 8.—Case No. 8a.—Forty days after operation, showing union of fragments. Compare with case No. 8, Fig. 5.

CASE No. 8a.—Control of Case No. 8.

A fragment of bone, one-quarter inch in length, was removed from the shaft of left radius.

Radiographic findings:

1. Second day after operation—roentgen rays shows gap of one-quarter inch in radius. (See Fig. 6.)

2. Twenty-five days after operation. There is evidence of a slight amount of bone proliferation. (See Fig. 7.)

3. Forty days after operation, union of fragments is shown. (See Fig. 8.)

In the foregoing experiments, it was found that bone growth was in no degree inhibited by the use of the roentgen ray. In fact, in Case No. 8, after a series of five massive exposures, complete union was shown forty-three days after operation, and proliferation even greater than occurred in its control on which the roentgen ray was not used, save for short exposures in the aim of obtaining radiographic findings. (See Figs. 5 and 8.)

It not infrequently results that a pure investigator, working along laboratory lines and not meeting clinical problems, goes far astray, and, in some instances, an excellent piece of research has come to naught owing to the fact that it was founded upon false premises. Illustrative of this is a report⁶ of animal experimentation with fragmented bone grafts, recently published, in which that author introduces his paper with the following erroneous statement, as a premise:

"The bone (forearm) is too small to maintain a transplant in position by the use of a Lane plate or other device; and the insertion of an intramedullary splint with a dowel is a procedure of considerable difficulty and requires a large exposure of the fractured bone. In performing bone transplant operations in dogs while pursuing the study of bone repair, the writer was struck with the universally good results obtained by transplanting small bone fragments 1 to 2 mm. in size, to fill a defect in the shaft of the radius. Although this study is purely an experimental one, it is reasonable to assume from the results obtained that it will be of distinct clinical value in well selected cases."

The first statement, namely, that "the bone is too small to maintain a transplant in position by the use of a Lane plate or other device," is an unfortunate suggestion, since the Lane's plate should *never, under any circumstances*, be used as the fixative agent for the graft. The intramedullary splint, it is true, is not applicable in these cases; it is, however, an indisputable fact that the inlay graft, when properly inserted, affords an ideal fixation and an exceedingly promising prognosis. The most unfortunate part of that author's premise is his statement that, because by his method of placing small bone fragments in a hiatus freshly made in an animal's long bone, union was produced, it would be "reasonable to assume from results obtained that it would be of distinct *clinical* value in well selected cases,"⁶ in the treatment of pseudarthrosis.

The error of such conclusions, as the foregoing, can be no better emphasized than by a summary of our results obtained with rabbits in our attempt to determine the cause of pseudarthrosis. In our experimentations, we failed absolutely to produce a single case of pseudarthrosis, simply because we were unable to prevent the early

⁶ Bancroft, F. W.: The Use of Small Bone Transplants in Bridging a Bone Defect, *Ann. Surg.*, 1918, lxxvii, 457.

and rapid union of the fragments of the shafts of the long bones. In one series of our cases, discussed above (see *d.*), bone fragments were allowed to remain in the hiatus in precisely the same manner as described in the article quoted. Union in these cases, as has already been stated, occurred promptly whether the shaft fragments were splinted or not, and whether or not subjected to massive and frequent exposures to the roentgen ray. It is, thus, clear that the experimental findings, as set forth in the article above cited, can have no force, whatsoever, as argument for the *independent* use of osteoperiosteal grafts, in the clinical treatment of genuine pseudarthrosis, or malunion.

On the other hand, no one is more strongly convinced of the potency of fragmented, or osteoperiosteal, grafts as productive of bone growth, than the author, who, in experimental work as early as 1909 and 1910,¹ observed the unusual osteogenetic activity of such transplants. It is of interest, in this connection, to make reference to Case No. 5 (see Figs. 9 to 12), of our series of experimentations herewith reported. In this case, one slender fragment of bone was left in the hiatus formed by removal of about one-quarter inch of substance from the shaft of the radius. In striking contrast to those cases in which *all* particles of bone were removed from the gap at first operation (see Cases No. 8 and *Sa*, Figs. 3 to 8), this case showed a remarkable and rapid bone proliferation at the end of twenty days. Furthermore, by the thirty-first day, not only was there complete and solid union, but the gap was entirely filled with new bone. In cases in which all fragments were removed, a period of about forty-two days seemed required for union. The remarkable osteogenetic activity manifested in Case No. 5 was, of course, due to the presence of additional bone surfaces containing the potent bone-growing cells, namely, the fragment which originally remained, spanning the hiatus in the shaft of the radius. This bridge of bone functionated in the identical manner of an osteoperiosteal, or fragmented graft.

The value of the osteoperiosteal, or "sliver" graft, as a means of furnishing further foci for bone growth, has been repeatedly demonstrated, not only in the author's animal experimentations, but more particularly in the application of these grafts as supplements to the main fixation graft in his series of nearly 2000 cases of bone transplantation on the human subject. However, emphasis should be laid on the fact that in all clinical cases of pseudarthrosis, with or without loss of bone, such grafts should be employed *only as supplemental* to the main fixation graft which must be so inserted as to lie in generous contact with the primary source of blood supply and nourishment to bone, namely, the marrow cavity, or the cancellous bone structure. This can only be satisfactorily accomplished by the inlay method. The definite limitations to the use of fragmented, or osteoperiosteal, grafts have never been more convincingly demon-

strated than by recent reports from American and European surgeons of the failure of these grafts, when used alone, to secure union in cases of pseudarthrosis.

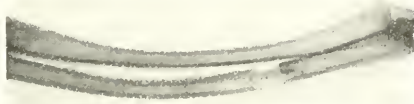


FIG. 9.—Case No. 5.—Five days after operation, showing the removal of about $\frac{1}{4}$ inch of the shaft of the radius. Note that in this case a slight bridge of bone has remained, spanning the gap between the shaft fragments.

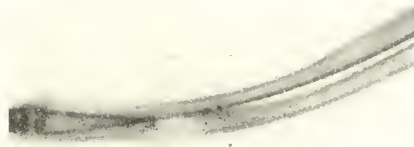


FIG. 10.—Case No. 5.—Twelve days after operation. There is slight evidence of bone growth. (In this figure the film was reversed in printing.)



FIG. 11.—Case No. 5.—Twenty days after operation. Note the remarkable proliferation which has taken place. The original hiatus is nearly filled with new bone.

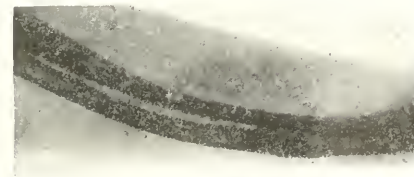


FIG. 12.—Case No. 5.—Thirty-one days after operation. The gap is completely filled with new bone and there is firm union. Compare the progress of bone growth in this case with that of case No. 8 (Figs. 3 to 5) and its control, case No. 8 a (Figs. 6 to 8). In both of these latter cases, there was complete removal of all fragments from the hiatus in the shaft of the radius. Note the striking contrast between these latter cases and case No. 5, in their respective radiographic findings. The remarkable osteogenetic activity demonstrated in Case No. 5 was due to the presence of the original bridge of bone left in the hiatus.

CONCLUSIONS.

1. In none of our experimentations with rabbits were we able to produce pseudarthrosis by repeated massive exposures to the roentgen ray, by removal of bone, nor by various degrees of splinting.

In every case, even when portions of the radius were removed to the extent of one-fourth of its entire length, we were prevented in our purpose by the early and rapid union of the shaft fragments, it being a well-known fact that bone growth in animals is much more rapid and constant than in the human subject.⁷

2. Frequent, massive exposures to the roentgen ray of fractures, with or without loss of bone, in no wise inhibited callus formation.

Following the suggestion that the common usage of the roentgen ray might play some role in the production of pseudarthrosis, series of fracture cases, with and without loss of bone, were subjected to long and repeated exposures. Comparison with a control group, on which the roentgen ray was not used, save for brief exposures incidental to observation of progress, showed that there was no difference in length of time required for the union of the bones in the two series of cases. Apparently the roentgen ray exerts no appreciable influence upon bone growth.

3. In cases of fracture, with loss of bone, in which *all* bone fragments were removed from the hiatus in the shaft of the radius, the average length of time for union was forty-two days.

Those cases of fracture in which the fragments were allowed to remain in the hiatus, showed a much more rapid and complete union, than occurred in the foregoing group. In one case of fracture, with loss of bone, in which one fragment was left bridging the gap, remarkable osteogenetic activity was manifest, complete restoration of continuity of the shaft occurring at the thirty-first day. This latter case affords a further demonstration of the value of the osteoperiosteal, or "sliver", graft, when used as a means of furnishing additional foci for bone growth.

⁷ In this connection, it is worthy of note that in many of the infected cases of fracture, with or without loss of bone, seen in the wards of this hospital, pseudarthrosis occurred, whereas, if the same relative amount of bone tissue be removed from a long bone of a rabbit, regeneration has been fairly rapid and complete.

POINTS IN THE PHARMACOLOGY OF CERTAIN DRUGS USED FOR STOMACH EFFECTS.¹

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ATROPIN.² This drug has such a decided action on certain secretions and certain motor functions of the body that it has for long years been assumed to have similar effects in the stomach. Yet clinical beliefs that have been supported by the leaders in medicine have so often been forced aside when the light of experiment has been turned upon them, that it behooves us to appraise carefully the value of such a drug as atropin in its application to the stomach.

1. *Secretion.* Observations on human subjects have been made by Crohn with the fractional method of gastric analysis. Some of his results were:

(a) *In Hyperacidity Cases with Normal Secretion Period.* One mg. ($\frac{1}{65}$ grain) of atropin sulphate administered to the patient hypodermically three-quarters of an hour after the meal, had little or no effect except that in the last one-half hour there was a rapid rise in acidity to 76 at a period when the control showed an acidity of 32. A similar experiment on another patient gave practically the same results. Doses by mouth sufficient to give signs of belladonna-poisoning (dry mouth, dilated pupil, etc.), raised the average acidity from 35 to 51.1. In all cases the motility was unaffected.

(b) *In Cases with Continuous Secretion.* In the control test a highly acid gastric juice persisted to the end of the experiment, six and three-quarter hours, though all the food had left the stomach at two and three-quarter hours. After the food had disappeared the acidity was higher than before, reaching 118 at four and one-half hours. The average total acidity was 89.

The next day with the same patient, all food having left the stomach at two and one-quarter hours, 1 mg. of atropin sulphate was given at this time hypodermically, and at one hour later the secretion had ceased. In the same patient fully atropinized by mouth for

¹ Presidential Address at the Twenty-second Annual Meeting of the American Gastro-Enterological Association, Atlantic City, N. J., June 9 and 10, 1919.

² Auer and Meltzer: *Am. Jour. Physiol.*, 1906, xvii, 17.

Barelay, A. E.: *Alimentary Tract*, 1915, p. 17.

Crohn, B. B.: *Am. Jour. Med. Sc.*, 1918, clv, 809.

Cushny, A. R.: *Pharm. and Therap.*, 1915, p. 323.

Ginsburg and Tumpowsky: *Arch. Int. Med.*, 1918, xxii, 553.

Ochsenius, K.: 1915.

Rehfuß, M. E.: *Tr. Am. Gastro-Enterol. Assn.*, 1918, p. 25.

Smith, Maurice I.: *Am. Jour. Physiol.*, 1918, xlvi, 232.

Zunz and Tysebaert: *Jour. Pharm. and Exp. Therap.*, 1916, viii, 325.

three days the stomach was free from food at three hours and the secretion ceased at three and one-half hours. The average total acidity was 60 as compared with an average of 89 in the control, but in this case the averaging of acidities does not make a valid comparison, because in the control the highest acidity was reached during the period of continued secretion, *i. e.*, after digestion was finished, a period in which there was no secretion at all after atropin. In this case exploratory laparotomy had shown no lesion.

In a second case the secretion was still continuous at five and three-quarter hours when the experiment was stopped. The average total acidity had *risen* from 85.3 to 94, the motility being unaffected. Then tincture of belladonna, 1 c.c. four times a day, was given by mouth for three days, when poisonous symptoms appeared. In a test at this time the secretion ceased at three hours, but the average acidity increased from 85.3 to 104.5.

We find then failure of atropin to lessen digestive secretion, and in continuous secretion cases a failure to act except after the digestive period. Then it had an effect only if given by hypodermic in maximum doses, or if previously given by mouth to the stage of poisoning. It actually increased the acidity of the digestive secretion and showed an inhibitory effect only on the abnormal continued post-digestive secretion.

In regard to the psychic secretion I have only the report of Rehfuess. In the early morning each of a number of men with a fractional tube in his mouth was set in front of a beefsteak and compelled to cook it though not allowed to eat it. The stomach secretion, withdrawn at intervals, ceased at sixty to eighty minutes and ran as high a total as 240 c.c., with average acidity of 97.2. In large doses by hypodermic atropin cut down the acidity and the amount of secretion, but never caused complete disappearance of the secretion. It is possible that the drying effect of atropin in the nose, mouth and throat and the sensory effect of blunting the sense of smell may have been important in the result.

2. *Motor Functions.* From a therapeutic point of view the only desired action of atropin on the motor functions is to overcome tetanic spasm at the cardia, at the pylorus and at the site of an hour-glass contraction.

Working with strips from the antrum, pre-antrum, body and fundus of the stomachs of rabbits, cats and dogs, Smith found that solutions of atropin sulphate 1 in 1,000,000 and 1 in 100,000 invariably produced relaxation, whether the strips were from the longitudinal, the circular or the oblique muscles. He obtained the same effects on the pyloric and cardiac sphincters. Zanz and Tysebaert, working on the stomachs of dogs one-half hour after hypodermics of from 0.005 to 1 mg. per kilo, found the contractions weak and diminishing in strength, the effect in some cases persisting five to six hours. After 0.001 mg. per kilo the movements were normal,

though the tone rapidly fell. Auer and Meltzer have demonstrated that these effects are due to paralysis of the vagus terminals at Auerbach's plexus.

I have not worked with stomach strips, but in experiments done with Dr. C. C. Lieb, using strips of the longitudinal muscle of the small intestine of dogs, atropin in large amounts completely abolished the tetanic contraction or cramps brought out by physostigmin and restored the peristaltic waves, but not the normal tone waves. From the work of others it is established that the same action takes place in the stomach. Ginsburg and Tumpowsky, for example, found that hypodermics of $\frac{1}{80}$ to $\frac{1}{40}$ grain invariably in five to ten minutes inhibited the tetanic contraction produced by pilocarpin and physostigmin in the stomach and restored the normal peristalsis. The inhibition was sudden and decisive and persisted for hours. The same results were obtained in the isolated stomach.

This conquering of tetanic spasm by atropin in doses which permit the vagus and splanchnic nerves to continue their ordinary influence on peristalsis has led Cushny to surmise that these abnormal contractions, such as are seen in pylorospasm and colic, arise from some mechanism distinct from that which presides over ordinary peristalsis. This action on abnormal tetanic contractions is indeed *the only possible motor effect of therapeutic amounts of atropin*. It seems therefore essential to distinguish the two known motor effects, viz., that of abolishing abnormal spasmodic contractions and that of abolishing the tone of the whole stomach wall. Only the former is possible or desirable therapeutically, and in all probability it is not accomplished by paralysis of the vagus endings.

Clinically and in roentgen-ray work, atropin has been much employed to overcome abnormal tetanic contractions. On cardio-spasm, which it is agreed is not a true spasm, the drug has little or no effect. In röntgenology it is quite generally employed to overcome pylorospasm and the spasm of hour-glass contraction. From fluoroscopic observations, A. E. Barclay reported that after the dose of atropin the spasm often let up quite suddenly, but in some cases the drug was without effect. From a number of roentgenologists I have learned that quite frequently even large doses are without effect on pylorospasm. These men do not use small doses, but are accustomed to the employment of 1 to 1.2 mg. ($\frac{1}{65}$ to $\frac{1}{50}$ grain) of the drug, and that hypodermically, or some of them attempt to atropinize by two or three days' dosage. Within a few weeks I have had a case operated upon for cholelithiasis in which the roentgenologist, finding an hour-glass stomach that did not change after a hypodermic of 1 mg. of atropin sulphate, insisted on a diagnosis of ulcer with cicatricial contraction. But at the operation there was no sign of either hour-glass or ulcer.

In Czerny's pediatric clinic, Oehsenius found that in infants

enormous doses were necessary to overcome pylorospasm. For instance, in one child, a month old, to permit proper feeding, he had to keep up intermittently for ten weeks an atropin dosage of 0.15 mg. ($\frac{1}{33.5}$ grain) five or six times a day, and in another, three weeks old, had to give the same dose eight times a day for a whole week. There is much evidence of the ineffectiveness in pylorospasm of any but large doses at any age and in adults of the ineffectiveness of any but hypodermic doses; even then the relaxation is frequently not obtained.

Summary. 1. *Acidity and Secretion.* 1. In the ordinary hyperacidity case with cessation of secretion at the usual time, atropin or belladonna in maximum doses, either by mouth or hypodermic, has no useful effect on acidity or secretion.

2. In cases with continuous secretion a maximum dose by hypodermic half an hour before the meal did not lessen the acidity or secretion of the digestive period, but resulted in a stoppage of the secretion in a reasonable time after the food had left the stomach. A similar maximum dose at the end of the digestive period stopped the secretion in one hour.

3. In cases with continuous secretion, repeated maximum doses of the tincture of belladonna by mouth for three days caused a pronounced increase in acidity during the digestive period, but a cessation of the secretion after the food had left the stomach.

4. The psychic secretion is lessened, an effect not sought in therapeutics.

5. The natural secretion of mucus is not affected.

We find then a complete failure of atropin to affect hyperacidity favorably and a failure to diminish secretion except in continuous secretion cases. In these cases it does not depress and may even increase acidity and secretion during the digestive period, and it checks the continuous secretion only when given by hypodermic in maximum doses or when previously given by mouth to the stage of poisoning.

II. *The Motor Functions.* 1. Atropin can exert two kinds of motor effects on the stomach: (a) the abolition of tone in the whole stomach wall including the orificial sphincters, by action on the vagus myoneural junctions, and (b) the abolition of abnormal spasmodic contractions, as in pylorospasm, this effect probably not being dependent upon any action on the vagus terminals.

2. The latter effect is the only desirable one in therapeutics. It is a possible effect in some of the cases only, and then only from maximum doses.

3. So far as I know the action of atropin on hunger contractions has not been studied.

Conclusions. 1. In hyperacidity cases atropin has no useful effects in any dosage.

2. In continuous hypersecretion cases it may check the secretion after the digestive period, but it does this in maximum doses only.

3. In pylorospasm it may be useful, but in maximum doses only.

4. In the doses usually employed it is wholly without effect on the secretory or the motor unction of the stomach.

PEPSIN.³ By the U. S. Pharmacopœia test, with 1 in 3000 hydrochloric acid at 125.6° F. (52° C.), pepsin is required to digest 3000 times its own weight of coagulated egg albumen in two and one-half hours, *i. e.*, 1 grain of pepsin can digest at least 6¼ ounces. Prof. Gies, of Columbia, tells me that a specimen has been prepared 200 times as strong as this, *i. e.*, 1 grain can digest 600,000 times its weight. What a wonderful substance to have so little use in medicine! It is inactivated by hydrochloric acid above 0.5 per cent. strength (U. S. P.), 0.7 to 0.9 per cent. (Hamburger and Halpern), and by sodium chloride solution of 2.5 per cent. strength. It is not only inactivated but is destroyed by alkalis, for example, disodium phosphate in ½ per cent. strength (Hamburger and Halpern), sodium hydroxide in 0.01 per cent. strength (Sollmann) and sodium bicarbonate and carbonate, magnesium carbonate and lime-water (Hamburger and Halpern), when in sufficient amounts to make a persistent alkaline reaction. In the light of this destruction one wonders how Abderhalden and Meyer were able to find active pepsin in all parts of the small intestine, and to suggest that this pepsin would be active in the digestion of protein wherever the intestinal contents should become acid.

In the stomach contents, Wiltrup found it absent or below normal in every one of a thousand cases of achylia gastrica. Hernando and Alday found it absent in 3 cases and present in only very small amounts in 16 out of 22 cases of gastric cancer and in normal or above normal amounts in 65 cases of hyperchlorhydria, 37 cases of gastric or duodenal ulcer and 85 cases of cicatricial stenosis of the pylorus.

It is evident then that the only possible cases for the use of pepsin in therapeutics would be those of subacidity and achylia, whether cancerous or not. Its need is doubtful, but since pepsin digests protein only when this has been changed to acid albumin, if used at all it should be accompanied by a sufficient quantity of hydrochloric acid.

Pepsin preparations regularly have a milk-coagulating power. Whether this is due to admixture of rennin or because pepsin and rennin are one and the same enzyme is a still unsettled question among physiological chemists.

RENNIN.⁴ Rennin is not a digestant, but it has the power to coagulate from 5000 to 166,000 times its weight of milk in from one

³ Hamburger, W. W., and Halpern, B.: Arch. Int. Med., 1916, xviii, 228.

Hernando, T., and Alday, T.: Siglo Med., Madrid, March, 1917.

Wiltrup, G.: Hospitalstidende, August, 1916.

⁴ Harris: Jour. Anat. and Phys., 1894, xxix, 188.

to several minutes. The rennin curd uses up 13 per cent. more calcium phosphate than the curd from hydrochloric acid (Harris) and is less dense and more readily acted upon by pepsin.

The function of rennin in the gastric juice is therefore to retard milk in the stomach by changing it to a solid and to favor the digestion of its coagulable protein.

But in a medium strongly acid or more than slightly alkaline the rennin will not act. Therefore, on the one hand, in hyperacidity cases the curd formed is regularly the dense and comparatively indigestible acid curd and not that of rennin; and on the other the addition to milk of more than a very little lime-water or sodium bicarbonate, or as little as 2 grains of sodium citrate to each ounce will prevent the rennin coagulation, and will keep the milk in its liquid and less digestible form. In highly acid stomachs, however, it may take considerable alkali to prevent the undesirable acid coagulation of milk.

If we add rennin to milk just at the time of swallowing, may we not find this a useful remedy (1) in achylia cases with diarrhea, to coagulate the milk and so prevent its too rapid passage into the intestines, and (2) in hyperacidity cases to forestall the undesired acid coagulation?

HYDROCHLORIC ACID.⁵ The known functions of this acid in the normal animal are:

1. To favor protein digestion and the disintegration of connective tissue.
2. To induce closure of the cardia.
3. To establish a normal intermittence of opening and closure of the pylorus.
4. To serve as antiseptic.
5. To aid inversion of the disaccharides.
6. To form secretions to stimulate the production of pancreatic juice and bile.

That the absence of hydrochloric acid is quite compatible with

⁵ Army, H. V.: *Practice of Pharmacy*, 1918. Crohn, B. B.: *AM. JOUR. MED. SC.*, 1918, clvi, 656.

Ginsburg, Tumpowsky and Hamburger: *Jour. Am. Med. Assn.*, September 30, 1916.

Goiffon, R.: *Arch. Mal. de l'Appar. Digest*, 1918, ix, 262.

Horner, C. P.: *Jour. Am. Med. Assn.*, December 8, 1917.

Jones, N. W.: *Am. Jour. Med. Sc.*, 1918, clv, 335.

Joubert: Quoted by Goiffon.

Leo: *Die Salzsäuretherapie auf Theoretische und Praktische Grundlage*, Berlin, 1908.

Long, J. H.: *On the Physiological Activity of Combined Hydrochloric Acid, Investigations of the Therapeutic Research Committee of the American Medical Association*, 1915, vol. iv.

Marriott, W. McK., and Howland, John: *Johns Hopkins Hosp. Bull.*, 1918, p. 284.

Rehfuss, M. E.: *Jour. Am. Med. Assn.*, 1917, lxi, 1328.

Spencer, Meyer, Rehfuss and Hawk: *Am. Jour. Physiol.*, 1916, xxxix, 459.

Stehle, R. L.: *Jour. Biol. Chem.*, 1917, xxxi, 461.

fair health and the maintenance of nutrition is proved by the frequency with which the existence of achylia gastrica is discovered after only insignificant symptoms or no symptoms at all. I found achylia present in one girl, aged seventeen years, with complete lack of gastric symptoms, having tested her stomach merely because her grandmother and her mother had shown achylia. For hydrochloric acid as a remedy only one use can be suggested, viz., to replace a deficiency of acid in the gastric juice. Whether introduced acid can so serve is our question.

1. *Protein Digestion.* It is an established fact that for pepsin digestion of protein, acid is necessary. Therefore in an achylia case, if we are to have any digestion of protein in the stomach, we must supply hydrochloric acid as well as pepsin. Experiments done without pepsin regularly show a fair formation of acid albumin and thus give hope that the addition of pepsin may ensure at least some degree of gastric protein digestion.

Crohn, in fractional experiments on man in achylia cases, both simple and those of pernicious anemia, found that it was not possible to have a sustained acidity from mouth doses unless these were frequently repeated during the digestive period. To mention some of his experiments, in an *emptied fasting stomach* he placed 40 minims of diluted hydrochloric acid mixed with 100 c.c. of water. The immediate acidity was: Free 32, total 40. Successive specimens withdrawn at five-minute intervals showed rapidly diminishing acidity until at twenty-five minutes the titer was the same as before the acid had been given. When he administered 30 minims of diluted hydrochloric acid with an oatmeal test-breakfast the free and total acidities at fifteen minutes were 8 and 20 and at thirty minutes 12 and 18, but at forty-five minutes and thereafter had returned to 0 and 10 or thereabouts, the same as in the control experiment.

Then he administered repeated instead of single doses of the acid. Ten minims of the diluted acid every half hour during digestion gave a mild but definite rise in acidity which was sustained for one and three-quarter hours, and 10 minims every quarter hour raised the average total acidity from 20 to 55. The emptying time was unchanged.

Leo, quoted by Crohn, gave achylia cases large doses of hydrochloric acid, equivalent to from 75 to 225 minims of U. S. P. diluted hydrochloric acid, and obtained increases in total acidity but rarely any free acid.

Spencer, Meyer, Rehffuss and Hawk introduced strongly acid solutions (0.542 and 0.4 per cent.), and found that the gastric contents had returned to normal at the end of one hour. This they attributed to a rapid emptying due to the acid and a progressive neutralization of the excess of acid.

Rehffuss found that 10 or 15 minims of hydrochloric acid, properly

diluted, made no detectable change in the gastric chemistry. However, with a constant supply of acid for two hours by a Murphy drip at the rate of 200 c.c. of 0.25 per cent. acid per hour, equivalent to 5 c.c. of diluted hydrochloric acid per hour, the curve of secretion rose to 33 per cent. of normal, though there was at no time any free acid.

All these findings indicate that if we can only give enough hydrochloric acid by mouth, we can at least hope to change our albumin to acid albumin and thus prepare it for pepsin digestion. But acid alone is practically useless for the purpose of digestion, and to judge of its merits as a remedy, it must have all the factors for its action. In other words, we must administer pepsin with it. Moreover, the products of the action of pepsin and hydrochloric acid on protein are themselves capable of exerting a strongly stimulating effect on secretion.

Sippy makes a calculation that for the adult allowance of 100 gm. of protein a day it would require 700 minims of diluted hydrochloric acid for full gastric digestion, and that on account of the sensitiveness of the mouth and throat to acid it would be impossible to swallow this amount. However, there is never, even in normal cases, full protein digestion in the stomach. Moreover, some proteins require less acid than others for digestion, *e. g.*, Hawk states that the best strength for the digestion of fibrin is 0.08 to 0.1 per cent., while the best for coagulated egg-white is 0.25 per cent. Joubert found in achylia cases that on giving hydrochloric acid at the same time as raw meat, connective tissue still appeared in the stools. From strengths of 30 to 40 minims in 100 c.c. of water Crohn noted the development of considerable mucus, presumably from some local irritant action.

2. *The Emptying Time of the Stomach.* That in achylia gastrica it is not infrequent to have a very rapid emptying time is well known. In 11 cases of pernicious anemia, C. P. Horner found that 6 had emptied at one hour and in only 1 was there food at the two-hour period. N. W. Jones in a study of achylia concluded that in a broadly built non-ptotic person achylia is usually associated with a too rapidly emptying stomach and in this class diarrhea is prone to occur; whereas in ptotic types the ptosis and atony prolong the emptying time even up to seven hours or more, and in this class constipation is the rule.

There is considerable clinical evidence that in a fair number of achylic diarrheas, hydrochloric acid is a successful remedy. May not this be due to the restoration of the normal pyloric closure through the acid reflex and the consequent retardation of the food in the stomach? This, it is to be remembered, is a desired effect only in those cases with rapid emptying and diarrhea, and it is to be avoided if possible in those cases with flatulence or constipation. Crohn found the emptying time normal after doses of acid, but he

does not state that any of his cases were of the diarrheal type. Goiffon states that 1.5 to 3 gm. of hydrochloric acid a day may act to cause pyloric closure and so retard the food in the stomach. Jones's experience with the use of acid tallies with that of the author. He says "many are symptomatically relieved by its use, while others experience increased sourness and stomach irritation."

It has been stated that in some achylia cases the diarrhea may be checked by the administration of pancreatin. May not part of the value of hydrochloric acid lie in its power to enhance the pancreatic secretion through the formation of secretin, and thus to ensure more thorough digestion of proteins in the intestines? For though achylia gastrica is not ordinarily accompanied by pancreatic achylia, yet for certainty of digestion the rapidly passed food may require abnormal amounts of the pancreatic ferments.

3. *The Antiseptic Action.* In an achylia case it is quite common to find pronounced intestinal putrefaction. In both diarrhea and constipation cases this may be attributed, in part at least, to the failure of the achlorhydric contents to arrest the development of gas-forming organisms and to destroy the sundry proteolytic and pathogenic germs, thus permitting their passage into the upper intestine. In diarrhea cases intestinal putrefaction might also be accounted for by the fact that the ferments have too short a time in which to break down the protein before it reaches the usual region of abundant germ life in the intestine, and so the protein furnishes pabulum for the bacteria of the colon.

4. *The Effect on Pancreatic Secretion and Bile.* It is a well-established fact that, in the normal case, the hydrochloric acid of the stomach is an important factor in the production of secretin which stimulates the secretion of pancreatic juice and bile. What takes the place of hydrochloric acid in the achylia case, which does not lack pancreatic ferment, has not been determined; but if, from introduced acid, free hydrochloric acid or combined acid, which is really a loosely combined protein salt, can be passed into the duodenum even for a few moments, may not this result in the formation in the normal manner of ample secretin, and so provide the normal stimulus for the production of pancreatic juice and bile?

Summary. In achylia cases, from experiments based on the introduction of hydrochloric acid alone, without its natural congener pepsin, it is evident that with single doses of swallowable strength the acid titer of the stomach contents may be distinctly raised even to the normal. The results that might be expected from this are: (1) Successful protein digestion in the stomach when sufficient pepsin is also introduced; (2) slowing of the emptying time of the stomach by reestablishment of the pyloric closure reflex; (3) restoration of the normal antiseptic action in the stomach; (4) the proper formation of secretins; (5) normal liquefaction of the stomach contents by the added fluid.

Possible drawbacks to its use are: The establishment of pyloric closure in an already slowly emptying stomach, the production of gastric irritation, and the development of a mineral acidosis from its daily use over long periods of time. That it can produce *acidosis* has been demonstrated in dogs by a number of observers, and recently in man by Marriott and Howland. They gave 500 c.c. of decinormal hydrochloric acid in one day to each of four normal men, who ate their usual diet. This amount would represent 273 minims of diluted hydrochloric acid, a very large amount. On that day there was a distinct increase in the ammonia coefficient in the urine and at the same time an increase in the titratable acid in about the same proportion. Thus in a single day from swallowable amounts in man ammonia was deflected from the usual course of nitrogenous metabolism and a certain degree of acidosis was produced.

Stehle administered hydrochloric acid to dogs by mouth and found an increased excretion of sodium, potassium, calcium and magnesium. In the case of sodium and potassium, however, a subsequent compensatory retention took place. It has been figured that among the other effects there is a loss of calcium from the bones.

It is of interest that Ginsburg, Tumpowsky and Hamburger found hydrochloric acid in 0.5 per cent. concentration to be without effect on the hunger contractions.

Conclusions. 1. In cases of achylia gastrica, whether or not accompanying pernicious anemia, a deficiency of acid may be partially overcome by hydrochloric acid medication.

2. For digestive purposes hydrochloric acid should always be accompanied by pepsin.

3. In the achylia with diarrhea, acid promises a more noticeable result than in the achylia without diarrhea.

4. When acid produces sourness and stomach irritation its use should not be continued.

5. To avoid acidosis alkalis should be given during the same period, though not at the same time as the acid, the amount required being judged by the effect on the urine reaction.

To avoid the trouble of frequent medication in cases of achylia gastrica I have found it a good plan to have the patient take at the main meal most of the putrefactive protein of the day, such as eggs and flesh foods, the allowance of which is small in these cases, and have the acid and pepsin taken with this meal only. For practical reasons liquid medicine cannot be taken for any length of time after the meal, but doses of 20 or 30 minims of diluted hydrochloric acid and a few grains of pepsin in a full glass of water may be taken with the meal and frequently at half and even one hour later.

THE SOLID HYDROCHLORIC ACID PREPARATIONS. In solid form there are marketed certain drugs purporting to contain hydrochloric acid available for digestive purposes. The best known are *oxyntin*,

a protein compound of hydrochloric acid, and *acidol*, which is chemically betaine hydrochloride. In a careful research under the auspices of the American Medical Association, J. H. Long found that acidol dissociates in an aqueous medium and supplies hydrochloric acid, but that oxyntin holds scarcely enough acid for the digestion of its own protein and cannot therefore supply any for other digestion.

NITROHYDROCHLORIC ACID. Nitrohydrochloric acid has frequently been employed by the older physicians. It is made by mixing hydrochloric and nitric acids, a violent reaction taking place, and the acids being split up to form nitrosyl chlorides and chlorine. There is a slight excess of hydrochloric acid, so that nitrohydrochloric acid of the U. S. Pharmacopœia is a liquid containing free hydrochloric acid, free chlorine and nitrosyl chlorides (Army). It hardly seems worthy of a place in the materia medica.

BITTERS.⁶ In Carlson's tests on a young man in good health, who had an esophageal obstruction and a permanent gastric fistula for feeding purposes, bitters were administered either by stomach fifteen to thirty minutes before meals or by mouth ten minutes before the meal. The patient was in the habit of taking his food by mouth, chewing it and then placing it in the stomach through the fistula. The bitters were the tinctures of gentian, quassia, calumba, humulus and condurango and the elixir of iron, quinin and strychnin. The tests numbered 50 with bitters taken into the mouth, 35 with bitters placed in the stomach and 50 without bitters for control.

When the bitters were taken by mouth they could not be retained long because of the salivation induced and had to be expectorated. Their effect on the appetite of this young man in good health was too slight to be of moment, though it was noted that at the evening boarding house meal, which was never relished, the effect of the bitters was to make an already undesired meal still more undesirable.

When the bitters were placed directly in the stomach small amounts were found to have no influence on the quantity of the gastric secretion or on the acidity or pepsin concentration of the gastric juice. When large amounts were used Carlson's results agreed with those of other observers that their action in the stomach itself was rather to retard than to increase the activity of gastric digestion.

With tests on healthy dogs Carlson further came to the conclusion that bitters acting either in the mouth or in the stomach have no effect on the secretion of the gastric juice.

In another series of experiments Carlson and his colleagues showed that bitters acting in the stomach alone have no appreciable influence on the hunger mechanism as distinguished from appetite,

⁶ Carlson, A. J.: *The Control of Hunger in Health and Disease*, 1916.

Hoppe: 1905, quoted by Moorhead.

Moorhead, L. D.: *Jour. Pharm. and Exp. Therap.*, December, 1915, p. 577.

and that when taken by mouth in the usual way they inhibit gastric tonus and hunger contractions in direct proportion to the intensity and duration of stimulation of the nerve-endings in the mouth. In other words, *in normal people*, so far as they influence the hunger mechanism directly the bitters cause inhibition or depression of hunger.

Arguing from these experiments Carlson takes the ground that the whole value of bitters in medicine is mental and that they are in the same class as an inert but widely advertised patent medicine. He thinks that their continued use depends on two beliefs of the patient, namely, that they will promote appetite, and that anything with a strong and bad taste is strong medicine and therefore good medicine.

On the other hand, Hoppe noted that in a sick dog the use of bitters was followed by an increase in the quantity and acidity of the gastric juice, and Moorhead found that while in normal dogs bitters had no influence on appetite and no influence on secretion or a depression of it; nevertheless, in dogs made cachectic by daily bleedings to produce a chronic anemia they caused a distinct and significant increase in both appetite and secretion. Placed in the stomach without touching the mouth they had no appreciable influence. Barisoff gave tincture of gentian to a dog with the end of the severed esophagus opening outside, so that substances swallowed did not reach the stomach. He followed this with a meal, and in 6 tests without the bitters and 6 tests with found that after the bitters the average amount of gastric juice increased 30 per cent. If he gave the bitters as long as twenty minutes before the meal this effect was not obtained. An excess of bitters checked the secretion.

I myself have noted in many cases of achylia gastrica that bitters have the power to create or increase appetite, though having no effect on the gastric secretion. And I would register my opinion that in many persons with subnormal nutrition, especially in those recovering from an acute illness, bitters have a real value in promoting appetite, and that this action is not dependent on the patient's belief in the efficacy of the drug.

Conclusion. A bitter is useful as an appetizer for those with subnormal nutrition, as in convalescence from acute illness, provided that it is taken not more than five to ten minutes before the time for eating. It acts in achylia gastrica as well as in cases with gastric secretion. In subacidity it promotes the secretion of gastric juice. It should be administered in just sufficient dose to give a strong bitter taste and not in amounts large enough to have a depressant action in the stomach. If the patient is in a state of normal nutrition, but psychically disturbed about eating, it will be useless. If the appetite is already normal the bitter may not only fail to increase appetite but may even lessen it. If the stomach and bowels are deranged bitters may nauseate. The effect on appetite is solely

the local one on the taste buds, therefore it cannot be obtained if the bitters are hidden in capsules or coated pills.

CERIUM.⁷ The oxalate, which is the one salt employed, was studied by Baehr and Wessler. They found that it is non-poisonous to dogs even in doses of 50 grams, and that its action is mechanical as a protective to the gastric mucous membrane. Administered in advance it would check the vomiting from a local stomach irritant, such as ipecac, but had no influence on the vomiting from a central emetic, such as apomorphine. They state that the drug is useless in the small doses usually administered and recommend that it be given in doses at least as large as those of the bismuth salts.

BISMUTH.⁸ The bismuth salts in common use are the subcarbonate, the subnitrate and the subgallate. The subnitrate is crystalline, and because of this fact probably less bland than the others, which are amorphous. Contrary to the general belief they are all without astringency, that is to say, they do not cause shrinkage of tissues with which they come in contact.

Being basic salts they have the power to take up acid. Theoretically, of *bismuth subnitrate* 1 gram will neutralize 2 c.c. of diluted hydrochloric acid, or the acid of at least 40 c.c. of gastric juice, with the formation of bismuth nitrohydrochloride. But the change takes place very slowly and Böckman has demonstrated that in such acid concentrations as are found in the stomach the subnitrate possesses but little acid neutralizing power. Of *bismuth subcarbonate*, 1 gram will neutralize 4 c.c. of diluted hydrochloric acid or the acid of at least 80 c.c. of gastric juice, with the formation of bismuth chloride. It does not change to bismuth oxychloride as so frequently stated, for this basic salt cannot form in an acid medium. Bismuth subcarbonate changes somewhat more rapidly than the subnitrate, but not rapidly enough to justify attributing any important part of its action to its acid neutralizing power.

In a study of test-meals with the addition of bismuth subcarbonate, and fractionally extracted every fifteen minutes, Crohn reported that 2-gram doses given directly after the meal caused a diminution in acidity without any compensatory increase (as found after alkalies) in the acid secreted. According to a published chart he administered the salt half an hour after the meal, and up to the one and one-half hour period found the acidity slightly higher than in the control. But at one and three-quarters hours he got an acidity of 40 as compared with 70 for the control, and at two and one-quarter hours 50 as compared with 68. There was a slight retardation in the emptying time. In a duplicate experiment with a slightly greater dose the acidity was depressed from 56.8 to 45.2

⁷ Baehr, G., and Wessler, H.: Arch. Int. Med., 1908, ii, 517.

⁸ Böckman: Arch. Exp. Path. und Pharm., 1916, lxxx, 140.

Böhme, G.: München. med. Wehnschr., 1908, lv, 89.

Crohn, B. B.: AM. JOUR. MED. SC., 1918, clv, 803.

without delay in emptying or any evidence of the secondary rise in acidity which regularly follows the administration during the digestive period of the alkalis and alkaline earths.

Some years ago, in a number of instances, I administered doses of 2 grams of bismuth subnitrate just before or just after the test-breakfast, and though at the end of the hour the stomach contents usually showed a lessened acidity, and also a lessened secretion as determined by the Matthieu-Rémond method, there were a few cases in which the acidity was unchanged. Unfortunately, the protocols and the case records of these experiments were destroyed, so that I am not able to figure a reason why the bismuth should fail in these instances. In every case it was noticed that at the end of the test-breakfast hour the bismuth was uniformly mixed with the extracted stomach contents, and that it had changed from a heavy powder to a flocculent substance that settled slowly with the food. On two occasions I administered to dogs with their food, doses of 2 grams and 8 grams respectively of bismuth subnitrate colored red with carmin, and on removing the stomach and intestines three and seven hours later found the colored bismuth in this same flocculent and comparatively light state, partly mixed with the food residues, but mostly coating very uniformly the whole mucous membrane. In the dog killed at three hours it coated the stomach and small intestines throughout, except the first three or four inches of the duodenum. In the dog killed at seven hours it coated the whole jejunum and ileum. The coating stopped short at the ileocecal valve and there was no macroscopic evidence of bismuth in the colon.

Crohn's results with bismuth subcarbonate and mine with bismuth subnitrate would seem to be of the same nature, and would suggest that the action of either salt is not antacid but rather protective by coating the mucous membrane. Their power to spread over a large surface of membrane is almost phenomenal. Crohn's work establishes the fact that while the bismuth salts affect the secretions they do not essentially change the motility. By their protective action these bismuth salts would seem to have a value quite equal to that of cerium oxalate in preventing vomiting from local stomach irritants, such as ipecac.

Toxicology. By mouth the bismuth salts are not ordinarily poisonous, though Kohn reported the development of stomatitis and other manifestations of metallic poisoning from doses of 0.3 gm. (5 grains) given four times a day (length of time not stated). But poisoning from the use of a bismuth paste in the treatment of sinuses is not uncommon. One fatality resulted from less than 10 grams of bismuth subnitrate mixed with vaselin. Therefore, it may be conceived as possible that if the bismuth salt given by mouth should be retained on a raw area such as an ulcer, metallic poisoning may occur. As demonstrated by the roentgen rays such retention is unusual, but at our last meeting Jacob Kaufmann mentioned a case

of hematemesis to which Naunyn had given 25 grams of bismuth subnitrate, and in which at the postmortem von Recklinghausen took out of the crater of the ulcer 20 of the 25 grams of bismuth.

The symptoms have the characteristics of poisoning by the heavy metals, viz., stomatitis, salivation, a violet, blue-gray or blackish line on the gums, nausea, vomiting, diarrhea and prostration.

After bismuth subnitrate, but no other bismuth salt, another form of poisoning has occurred, namely, nitrite poisoning, this being due to the formation of nitrous acid. Most of these cases have resulted from the ingestion of large amounts of bismuth subnitrate for roentgen-ray work; but there are a few that have occurred from the medicinal use of the salt. Böhme, for example, reported that after giving an eighteen months marasmic infant several grams by mouth and two days later a similar dose by rectum, the child three hours after the last dose suddenly developed abdominal pain, diarrhea, cyanosis, and dyspnea, and died in half an hour. The blood and pericardial fluid gave tests for nitrous acid, and the blood for methemoglobin. Böhme found that when he mixed bismuth subnitrate with feces, nitrous acid was formed, and that when he placed this mixture in a rabbit's intestine, the urine showed nitrites. In one fatal case E. Meyer demonstrated nitrites in the urine, blood and pericardial fluid.

SILVER NITRATE. Before leaving the subject of drugs I wish to put on record a case of argyria that I have just found on my service, with a universal metallic slaty look to the skin, which came on after taking only $\frac{1}{4}$ grain of silver nitrate three times a day for two months.

I also this year had an autopsy on a similar case of argyria, in which the viscera were much discolored with silver deposits. This resulted from the application only once daily of a caustic silver stick to the mouth of a fistula. The period of application I do not know. This may point a moral for men who use silver nitrate in gastroenterology.

A ROENTGEN RAY SIGN OF PERINEPHRITIC ABSCESS.¹

BY M. H. FUSSELL, M.D.,

AND

H. K. PANCOAST, M.D.,

PHILADELPHIA

DURING the study of Case II in this report a curious fluoroscopic finding was observed which directly led to a diagnosis of perinephritic abscess, and which was confirmed by operation. The same

¹ Read before the Association of American Physicians, ²Atlantic City, N. J., June 18, 1919.

fluoroscopic sign was noted in Case I, but in this particular case the diagnosis was certain before the fluoroscopic finding was seen, hence no particular attention was paid to it except to note its presence. So far as either of us can discover this roentgen-ray finding has not been previously reported, though, of course, in the mass of literature a notice of it may easily have been overlooked.

CASE I.—F. H. W., male, aged thirty years, was admitted to the University Hospital, under the care of Dr. J. B. Carnett, October 2, 1916, with a diagnosis of renal calculus on the left side. The diagnosis was confirmed by roentgen rays and the stones removed by Dr. Carnett. The patient did well until October 10, when he developed fever of a mild type. On October 25 the fever became septic in type and continued until December 13, when a fluoroscopic examination showed fluid at the seat of the operation. This fluid was demonstrated while the patient was standing in the fluoroscope. The shoulders of the patient were grasped and the patient's body moved quickly two or three times from side to side. Watching the fluoroscopic picture showed a distinct wave in the supposed fluid. This observation was made by Dr. Pancoast. He offered the explanation that a collection of fluid was around the kidney, which showed the wave when agitated. The renal region was opened and a huge sac of pus demonstrated within the capsule of the kidney.

No other opportunity was given to discover whether this sign was an accidental one or whether it was common in subdiaphragmatic collections about the kidney on the left side until Case II was seen.

CASE II.—A. F., male, aged forty-six years, was seen with Dr. Shelly, of Ambler, Pa., May 14, 1918. The patient had been sick three weeks, was tired and chilly, and had fever of a septic type. He had pain referred to the base of the left lung. A paracentesis had been performed by Dr. Shelly, who had removed 3 or 4 c.c. of clear fluid with a needle from the base of the left chest. When seen by the writer there was pain and tenderness over the region of the left kidney, but nothing else could be detected. A needle was inserted in the left chest, but the tap was dry.

In the history which was obtained there were symptoms indicative of what was thought to be a peptic ulcer; a tentative diagnosis was made of subdiaphragmatic abscess from a perforating ulcer. He was sent to the University Hospital for a roentgen examination, but this was negative, and he returned the same day.

In a week after this his symptoms still continued; he was again sent to the hospital for careful observation. The symptoms were an irregular fever of septic type, with persistent but slight pain over the region of the left kidney. A roentgen-ray examination, with the patient lying on his back, showed the diaphragm to have the normal arch, and nothing particular could be seen. A plate taken, however, showed a beautiful picture of gall-stones, but did not reveal the presence of liquid. Remembering the experience with

Case I, the patient was placed upright in the fluoroscope and the first observation was that the left leaf of the diaphragm was flat and was immobile, and had lost its normal arched position.

The patient's shoulders and body were then moved quickly from side to side, and there was distinctly seen the same wave above the renal region which was observed in Case I. This observation was confirmed by both authors and by several other observers.

In view of these facts an exploration was advised in the left lumbar region, with the belief that all of the symptoms were due to a collection of pus in or around the left kidney.

Dr. A. C. Wood, who performed the operation, hesitated to explore the region because the local physical signs of a collection in that region were so slight, but urged that the gall-stones be removed and the lesser peritoneal cavity be explored. This, of course, was a rational opinion, but because of the curious fluoroscopic sign he was persuaded to open the kidney region. The incision showed the left kidney tightly bound down by its lower half. But surrounding the upper pole an abscess containing approximately 200 to 300 c.c. of pus was found.

The patient made an uninterrupted recovery and was discharged June 25.

On October 30 the patient developed marked symptoms of gall-bladder disease. He was again roentgenographed and the first plates showing gall-stones were confirmed. The gall-bladder was removed and showed thirteen stones. There was no evidence of previous or present collection of pus in the lesser peritoneal cavity. Today the patient is well.

This fluoroscopic sign is reported, because we believe it will be of value in certain obscure cases of fever, with suspicious signs about the left kidney, but which signs are not certain enough to warrant an exploration.

In Case I it will be noted the pus was within the capsule of the kidney; no note was made as to the shape of the diaphragm. In Case II the diaphragm had an entirely normal appearance when the patient was lying down and became flattened when the patient was upright. This phenomenon is not clear to us. We have thought of many explanations, but none seem satisfactory. It will be noted also that the amount of fluid was not large, which makes the sign of value in early cases. This second patient was soon relieved, having been in the hospital only about four weeks after operation.

Of necessity, pus about the right kidney will not be expected to give this sign, as the liver intervenes between the kidney and the diaphragm. So far as we know no such observations of collections of pus between the liver and the diaphragm have been made.

It is confidently hoped that other observers will search for the presence of a wave under the diaphragm in cases of subdiaphragmatic or perinephric abscess when the body is quickly moved from side to side.

EFFECTS OF RESTRICTED (SO-CALLED ULCER) DIETS UPON GASTRIC SECRETION AND MOTILITY.¹

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MEDICAL literature offers several studies of the clinical end-results of medical treatment of gastric and duodenal ulcers. The chemism and physiology of the stomach after operation has also been studied. But practically no information can be obtained regarding the direct results upon the stomach of the various forms of medical treatment. Whether clinical improvement during an ulcer cure depends upon a change in the chemistry and motility of the digestive organ remained until recently a matter of speculation rather than a demonstrated fact. The most illuminating articles on this subject are those contributed by W. W. Hamburger,² of Chicago. He was able to demonstrate (by radiographic means) during intensive medical treatment the actual healing of ulcers, the disappearance of "niche" phenomena and the restoration of normal peristalsis and motility. While he refers from time to time to changes in the chemistry of the organ as a result of restricted diet, his attention is focussed mainly on the radiographic picture of the healing ulcers.

J. Friedenwald and Baetjer³ carefully observed radiographically the function of the stomach during medical treatment. Their observations led them to conclude that several weeks, even months, of protracted diet were necessary before the disappearance of signs of abnormal function, such as exaggerated peristalsis, delayed motility, irregularity of contour, etc. The studies of Friedenwald and Baetjer are the first attempt directly to observe the effect of medical treatment on healing ulcers.

It is upon the chemism and the motility of the stomach while undergoing medical treatment that I am attempting to contribute some facts. This paper is based on observations made upon 34 patients. The cases belong in one general group; they were either proved instances of gastric or duodenal ulcer or they were cases suspected of bearing ulcers. In 5 of the patients ulcer was demonstrated by operation at a later date; in 21 of the cases ulcer was the

¹ It is a great pleasure to acknowledge with sincere thanks the kind privileges extended by the attending physicians of the hospital in the course of this study.

² *Am. Jour. Med. Sc.*, 1918, clv, 204.

³ *Tr. Assn. Am. Phys.*, 1903, p. 9.

clinical diagnosis, based upon the history, physical findings, chemical data and radiographic evidence. In the remaining 8 subjects the final clinical opinion was that they were suffering from a gastric neurosis or a functional disturbance of the stomach.

The symptoms which these patients presented in common were periodic attacks of heartburn, pain after meals, acid eructations, occasional vomiting and loss of weight. Practically in all these cases hyperacidity was chemically demonstrable, hypersecretion was frequently present and delayed emptying of the digestive organ was a prominent factor.

Since intra-abdominal diagnosis at its very best is conceded to be inaccurate and open to error, it is better in this study to consider the effects of the diet upon the chemistry of a diseased stomach *per se* rather than upon the ulcer when and if present. In this study no light is thrown upon the pathological changes that an ulcer undergoes during medical treatment. Only the immediate effects of the dietary restriction are studied. The observations extended, as a rule, over from two to five weeks in each case; the remote effects of medical treatment are not considered.

PROCEDURE. The routine examination of these patients upon admission consisted of a careful history and physical examination, extraction of fasting gastric contents, Ewald test breakfast and other chemical tests, stool examinations for occult blood and finally a thorough radiographic examination. A fractional test-meal to establish the type of curve was also performed. After the collection of all data the patient was placed upon a restricted diet for a period of from two to four or more weeks. During the period of observation, fractional test-meals were taken every few days. The type of the acid curve, its maximum height, its duration, the presence of hypersecretion, the emptying time, etc., were carefully noted for any changes that could be interpreted as due to the form of treatment being instituted. Clinical notes were made from time to time so as to ascertain a possible parallel between improvement in subjective symptoms and a change for the better in the disturbed chemism of the organ. The fractional test-meal was chosen as the best laboratory method for the demonstration of the phases of gastric digestion. By this method, so intimately associated with the name of Rehfuß, the height and duration of the acid secretion can be computed and plotted, evidence of pathological hypersecretion becomes manifest and the emptying time of the organ accurately estimated for a given and constant test-meal (oatmeal gruel in this study).⁴

BASIC PRINCIPLES OF SO-CALLED ULCER DIETS. There are certain general characteristics which are common to all forms of so-called ulcer diet. These are:

⁴ Crohn and Reiss: AM. JOUR. MED. SC., 1917, cliv, 857.

1. Administration of highly nutritious foods in small quantities, frequently repeated.

2. Neutralization of the free acid of the digesting stomach.

This is accomplished by administering high proteid foods, mainly milk, with the addition of eggs and later of cereals. Antacid salts are commonly employed to assist the neutralizing action of the foods.

An improvement in the motility of the stomach is sought in cases in which emptying time is delayed. In the series studied, patients were subjected either to a Lenhartz diet carried out without modification or to a diet similar to the one advocated by Sippy.⁵ In the diet as we administered it, milk and cream in small doses (2 or 3 ounces) were given hourly during the day for the first three days; cereals were then added twice daily. At the end of a week two eggs a day were added and puréed vegetables were gradually introduced. All forms of meat were withheld until the third week. Antacids in small quantities were given between feedings; bismuth was a constant component of these powders. Occasionally gastric lavage for food stasis was employed, though this was fortunately rarely indicated.

Before proceeding to discuss the general effect of such a diet upon the gastric chemism, let us study the individual chemical reaction which results upon the introduction into the stomach of these various foods. As a control one should keep in mind the normal curve of secretion, while employing oatmeal gruel as a test-meal or the usual Ewald test breakfast. Chart I demonstrates the reaction of a patient with a normal curve to a test-meal consisting of 240 c.c. of milk. One notes immediately the fact that milk causes a high total acidity (up to 128 c.c. $\frac{N}{10}$ sodium hydrate per 100 c.c.); that the height of the acidity is maintained for three or four hours; that free acid is present in larger quantities than usually met with in cereal or bread test breakfasts, and that the stomach takes considerably longer to empty itself. The acid-binding qualities of milk are apparent in only the first half-hour; thereafter to the end of digestion free acid is liberally present.

Compare this with the exaggerated effects of a combination of milk and eggs (Chart II). The total acid curve mounts still higher, reaching a maximum of 146 per cent.; free acid becomes evident after one and a half hours and is present in strong concentration during the remainder of the digesting cycle. Emptying time is, as a result, prolonged, even allowing for the large amount of test-meal given. A free hypersecretion of concentrated acid persists after the disappearance of the last traces of food.

The behavior of a cupful (280 c.c.) of clear bouillon, as recommended in the von Leube diet, is similarly interesting (Chart III).



CHART I

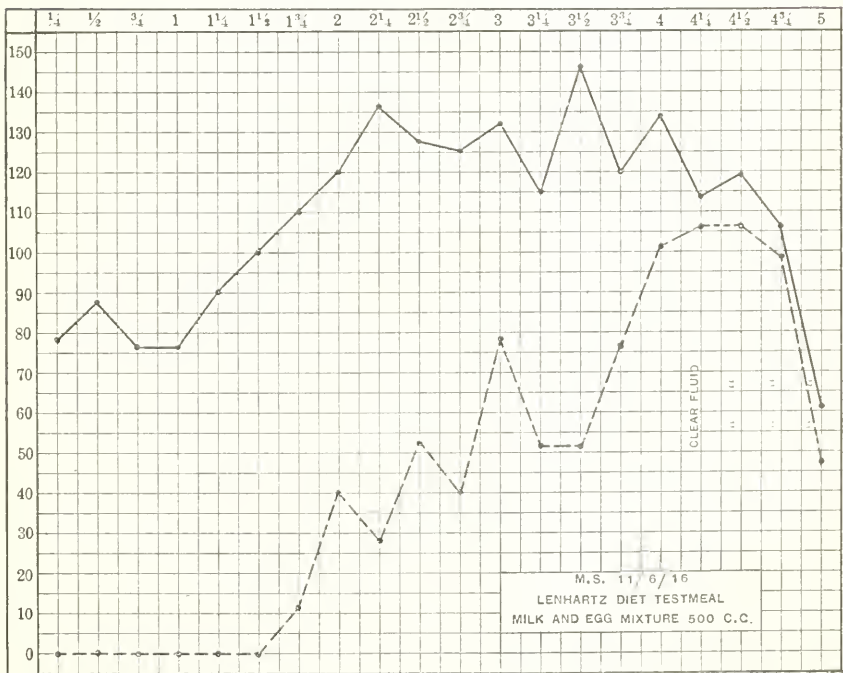


CHART II

No considerable binding of acid is at any time demonstrable. A high acidity, both free and total, quickly takes place and is maintained for two hours; thereafter the stomach is empty.

The conclusions to be drawn are: Milk is a strong acid stimulant and is only slowly emptied through the pylorus. The combination of milk and egg is a powerful stimulant to gastric secretion, causing a hyperacidity and hypersecretion, with prolongation of the emptying time. Bouillon fails to bind acid and is a mild digestive stimulant.

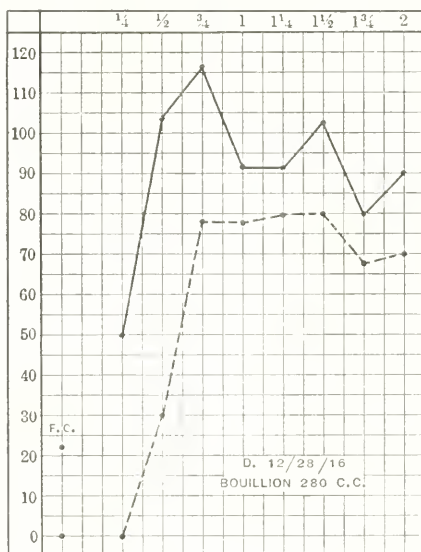


CHART III

The justification for the frequent repetition of food in small quantities is seen in Chart IV. Here we observe the effect upon the secreting organ of three ounces of milk repeated hourly. While the total acidity remains moderately high (average 80 per cent.) very little free acid is allowed to accumulate. As the free acid curve tends to rise toward the conclusion of each fifteen-minute period it meets the new portion of milk imbibed and is immediately neutralized. Since peptolytic digestion occurs only in the presence of free acid, it is apparent that in so far as actual splitting of the compound proteid molecule is concerned this stomach is really inactive.

If to this hourly administration of milk we add an alternating small dose of antacid salts (bismuth and bicarbonate or magnesia and bicarbonate in 5-grain doses of each as advocated by Sippy⁵), we are enabled to note (Chart V) that free acid entirely disappears and

that even the total acidity is strongly controlled, averaging only 43 per cent. Peptolysis is absent throughout.

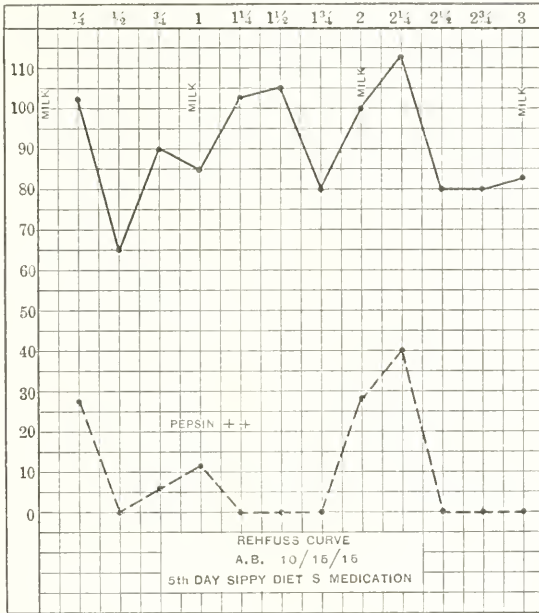


CHART IV

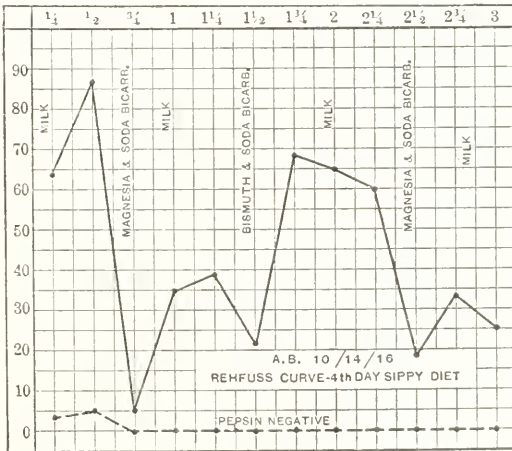


CHART V

If the reduction of total acidity and the complete neutralization or combining of free acid were the aims of this form of medical

treatment, then surely this plan of alternate milk and antacids fills all the requirements and offers the stomach the optimum conditions of anacidity for the cure of an ulcer.

However, of late much doubt has been thrown upon the hypothesis that ulcer of the stomach is due to the corrosive action of gastric juice. This theory really gained headway before the realization by the older clinicians of the fact that duodenal ulcer outnumbers in frequency gastric ulcers. The charted curve of acidity in the duodenum during digestion regularly fails to show the presence of any free acid, nor is the total acidity at any time high (Chart VI). The similarity between this chart and the preceding one is striking. Our approved methods of medical treatment aim to accomplish in

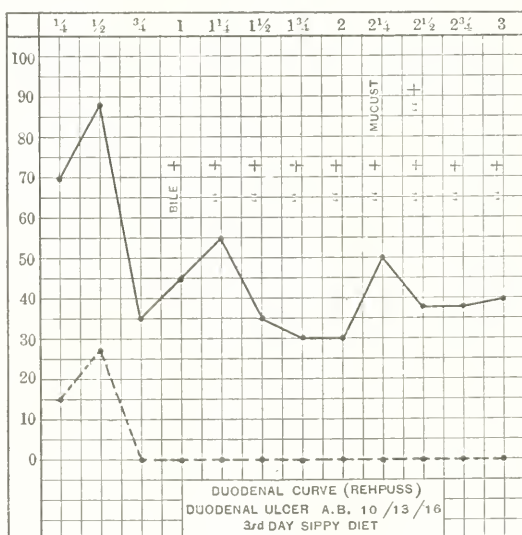


CHART VI

the stomach the very conditions of combined or neutralized acidity which are regularly and normally present in the so-called juxtopyloric portion of the stomach or duodenum. Yet under these very highly desirable and optimum conditions of anacidity duodenal ulcers appear and grow.

A closer study of the entire subject tends only to raise more doubts as to the *modus operandi* of cure of ulcers by medical treatment. The causal relationship between the hydrochloric acid and ulcer has not been proved, nor are we able unquestionably to accept the hypothesis that the cure of ulcer depends on the neutralization of the free acid of the stomach.

However, clinically, the beneficial results of medical treatment cannot be denied or gainsaid; it behooves us therefore to proceed to

study the effects of days and weeks of the administration of such a regimen on the gastric secretion.

EFFECT OF MEDICAL TREATMENT ON GASTRIC ACIDITY. Of the 34 cases which constitute the basis of this study 11 cases had an isosecretory or hyposecretory curve and 24 a hypersecretory curve of acidity (Rehfuss⁶). Let us assume that a beneficial effect of the medical treatment would be the diminution of an excessive hyperchlorhydria and a return to a normal or hyposecretory type of curve. In the series observed, medical treatment succeeded in causing a definite lowering of the acid curve in 6 of the 11 cases, with iso- or hyposecretory curves; 5 of the 11 were unaffected or unchanged. Of the cases with marked hyperacidity, numbering 23 in all, only 7 showed a lowering of the acid curve; in the remaining 16 the curve remained high in spite of persistent and rigid dieting and rest in bed.

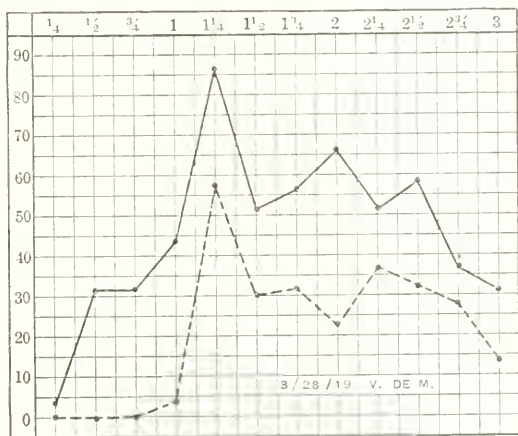


CHART VII

The lowering of the acid curve was often very marked, much more so in cases of hyperacidity than in those with normal or subacidity. Chart VII is the curve of a case of functional hyperacidity (operative findings negative) before the institution of treatment. Chart VIII the same case on the tenth day of a Lenhartz diet. The lowering of activity, diminution of hypersecretion and improvement in motility are marked.

Cases with normal curve of secretion, though suffering with symptoms of heartburn and belching, often show a similarly striking reduction of acidity to a subnormal or hyposecretory status.

Chart IX is the curve before treatment of a case of probable duodenal ulcer, with symptoms three years in duration; radiographically a persistent duodenal irregularity and stasis were visible.

Chart X is the curve of the same patient on the fourth day of a Lenhartz treatment, Chart XI on the seventh day and Chart XII

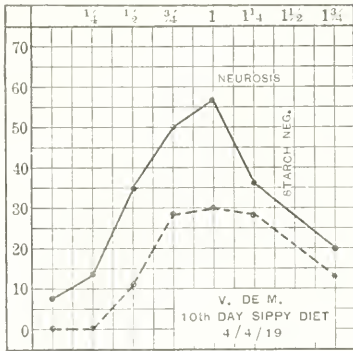


CHART VIII

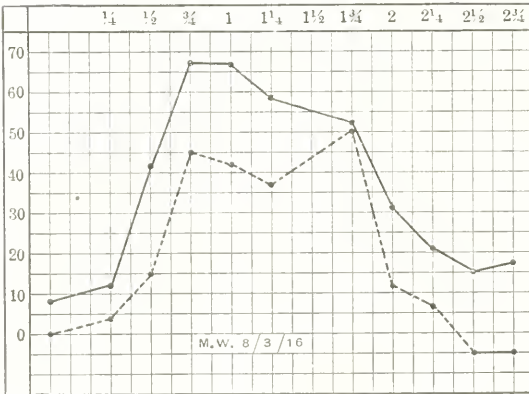


CHART IX

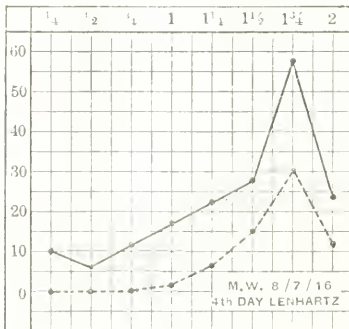


CHART X

on the twelfth day. The progressive lowering of acidity was accompanied by gradual improvement of subjective symptoms and disappearance of epigastric tenderness on pressure. This case, however, differs from the majority of the cases showing improvement, in that the reduction of acidity takes place as early as the fourth day of treatment. In most of the patients the chemical improvement was not demonstrable before the fifth to the seventh day. In more favorable cases the reduction of acidity began about the end of the first week of restricted diet and was maintained to the end of the period of observation. All of these cases but one were accompanied by marked relief from subjective clinical symptoms.

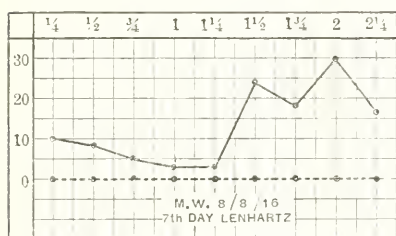


CHART XI

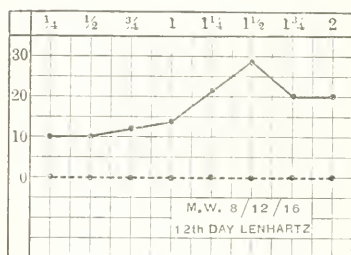


CHART XII

Of the 21 cases in which no reduction of acidity could be demonstrated little need be said; their curves resisted, many of them, even protracted restriction of diet, often meat-free for weeks. In spite of this more than half of these cases showed clinical improvement some of them markedly so.

The introduction of meat on the tenth day of the Lenhartz diet or the fourteenth day of the modified Sippy diet often converted a case which was tending toward diminished acidity into one with persistent hyperacidity. The following case is an illustration of this kind. The patient was one who had been suffering for seven months with symptoms of duodenal ulcer. A large indurated ulcer of the duodenum was in fact demonstrated at operation several months later. Chart XIII is the curve upon admission to the hospital (service of Dr. Manges).

Chart XIV the same on the fourth day of Lenhartz diet.

Chart XV the same on the sixth day of Lenhartz diet.

Chart XVI the same on the tenth day of Lenhartz diet, scraped beef having been given the patient for the first time on the previous day. The marked increase in acidity is noteworthy.

Chart XVII the same patient on the twelfth day of Lenhartz diet, meat having been removed from his diet. A slight improvement is noted.

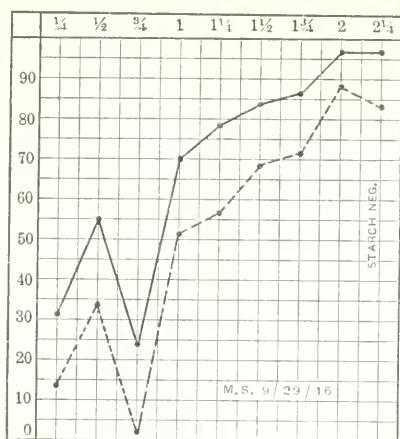


CHART XIII

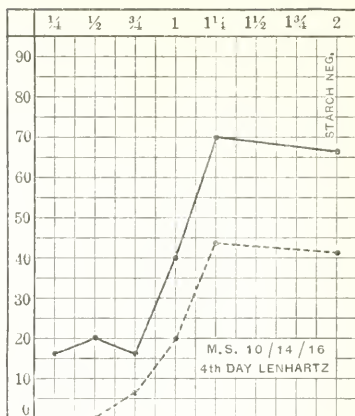


CHART XIV

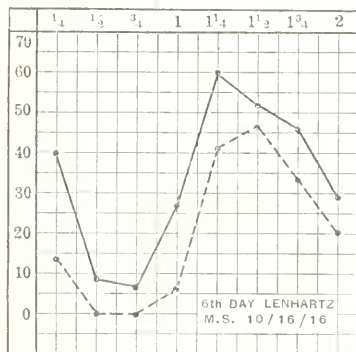


CHART XV

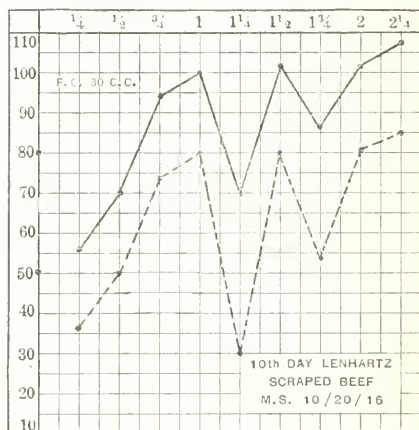


CHART XVI

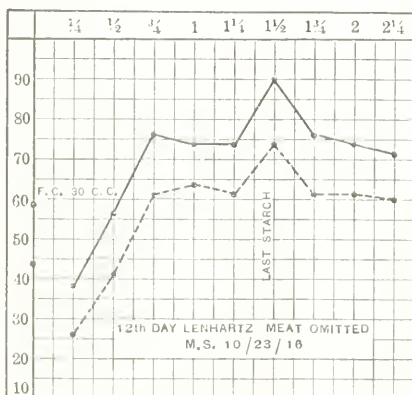


CHART XVII

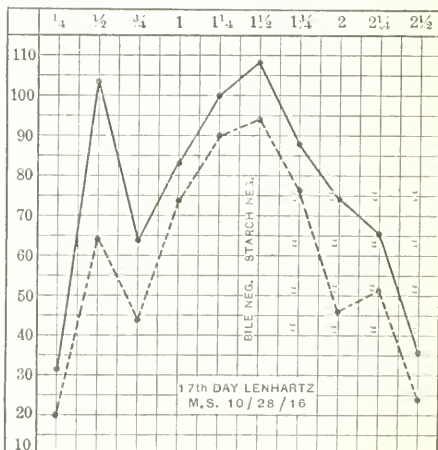


CHART XVIII

Chart XVIII is the curve on the seventeenth day of diet, still meat-free. Note the persistence of hyperacidity.

Repeated fractional tests of this patient were made up to the twenty-eighth day of the diet. (See Charts XIX and XX.) The hyperacidity hereafter failed to be reduced. The patient was discharged from the hospital free of subjective symptoms. Within a few weeks he returned with recurrence of his symptoms and was subsequently referred for surgical interference.

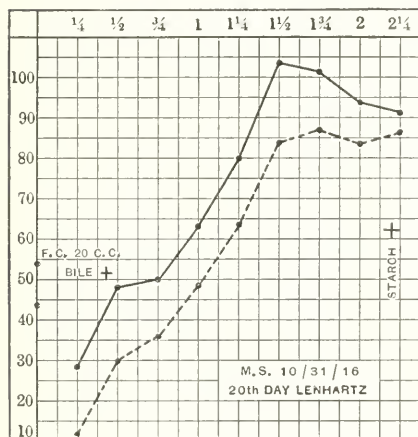


CHART XIX

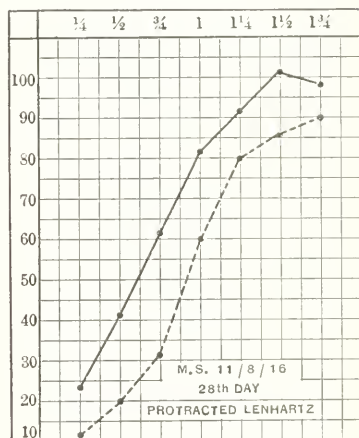


CHART XX

A vital question must occur to one's mind at this point. Is the reduction of hyperacidity which takes place during medical dietary treatment paralleled by clinical improvement, and conversely is a resistant hyperacid curve accompanied by persistent gastric symptoms?

Taking the cases as a whole 13 were chemically improved, 21 were not, a net chemical improvement of only 38.3 per cent. Yet clinically 25 of the 34 cases were discharged from the hospital free of symptoms, a percentage of 73.5 per cent., not quite as high as those presented by Lenhartz or von Leube, but still high. Of the 13 favorable cases in which the acid curve was reduced and the hyperacidity obliterated, 12 left the hospital symptom-free.

On the other hand, of the 21 cases with a persistent high acid curve in spite of treatment, 13, or 62 per cent., were markedly clinically improved. The remaining 38 per cent. (8 cases) left the hospital with the same curve as on admission, and clinically unimproved by their treatment.

A certain parallelism between chemical and clinical results is obvious.

TABLE I.

Acid curve, reduced, 13 (38 per cent.).
 Clinically improved, 12 (92 per cent.).
 Clinically not improved, 1.
 High acid curve, persistent, 21 (62 per cent.).
 Clinically improved, 13 (62 per cent.).
 Clinically not improved, 8 (38 per cent.).

The figures in heavy type are the interesting group, namely, those in which the curve remained acid-fast, and yet the patients left the hospital free of symptoms.

EFFECTS OF RESTRICTED DIET AND REST IN BED UPON GASTRIC HYPERSECRETION. The fractional test-meal is an ideal medium for the demonstration of hypersecretion. As the successive samples are removed from the stomach at quarter-hour intervals the proportion of food or cereal to the digestive fluid becomes smaller. With normal motility the last portion of the gruel disappears at two hours. It is at this time that hypersecretion when present becomes evident, for from this point one removes every fifteen minutes a sample of secretory fluid unadulterated by food. This is the pure secretion of gastric tubules; it is usually profuse so that large amounts can be removed, and it continues sometimes for several periods or even hours after the food has passed the pylorus. In exaggerated instances as much as 30 c.c. of pure acid fluid can be removed every five minutes.

The exact clinical significance of alimentary hypersecretion (we shall omit from present discussion continuous hypersecretion) has yet to be determined. Strauss,⁷ Zweig⁸ and others who noted the phenomenon described it as a pathological factor and ascribed its presence to the existence of an organic lesion of some part of the alimentary tract. Gastric or duodenal ulcer, chronic appendicitis or reflex irritation of gall-stones were and are all held responsible for the stimulation of this excessive fluid. But opinion is not uniform on the significance of its presence, and we need only quote Rehfuß,⁹ who in a recent article spoke of hypersecretion as being of no pathological importance and of its presence in several normal controls.

The period in the cycle of digestion in which hypersecretion is most evident is the period following the evacuation of the food. The titer of this hypersecretory fluid is usually high in acid, averaging from 60 to 80 per cent.; practically all of it is free acid; only a very small percentage is present as combined acid and practically none as acid salts. It is at this period that the pains of ulcer are often most marked; this remains true whether we ascribe the pains

⁷ Deutsch. Arch. klin. Med., 1895, lvi, 120.

⁸ Arch. Verdauungs., 1907, xiii, 143.

⁹ Jour. Am. Med. Assn., 1918, lxxi, 1535.

to the direct action of the excess of free acid upon the ulcer or the stomach wall or whether we attribute the pains to the exaggerated peristaltic waves or hunger contractions which become evident during this part of the digestive cycle.

Whatever the significance, hypersecretion is a common phenomenon in gastric and duodenal ulcer; it was present twenty times in this series of 34 cases, appearing toward the end of the period of food digestion as a postdigestive or alimentary hypersecretion.

We are interested in knowing what effect, if any, medical treatment, consisting of a marked restriction in food and rest in bed, has upon this factor. A close association is noted between hypersecretion and hyperacidity; 16 of the 20 instances of hypersecretion were in cases with gastric hyperacidity. In 9 of the 20 cases, where

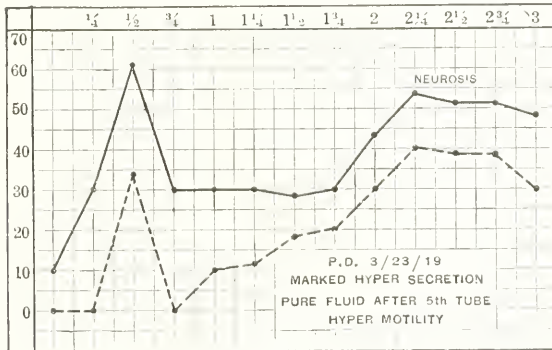


CHART XXI

present, hypersecretion was markedly improved or caused to disappear by medical treatment, a percentage of 45 per cent. In the other 11 cases, or 55 per cent., no effect was noted. The beneficial results of treatment were often very marked in this respect. Thus, for instance, Chart XXI is the curve of a case of gastric neurosis with hypersecretion, this curve being taken upon admission to the hospital, service of Dr. E. Libman. Chart XXII is the same case after six days of modified Sippy diet. Note that the character of the curve has changed; the acidity is somewhat higher but the hypersecretion is less marked, and the stomach empties itself in one and three quarter hours. Chart XXIII is the curve on the twelfth day of the diet. The curve is quite normal, the observation on the chart at the end of two hours being "scant secretion;" emptying time is normal. Many well-marked examples of the effect of medical treatment in causing the disappearance of hypersecretion could be demonstrated in the cases of this series. In fact, this is one of the most striking effects of medical treatment when a good result is present.

Much disappointment was felt in that the beneficial effect was not accomplished in a greater percentage of the cases. Eleven cases, or 55 per cent., were in nowise modified by either the restricted diet, the use of antacids or the physical and psychical rest accompanying the stay in the hospital. It is hardly possible to explain the failure in this not inconsiderable percentage of the cases.

Does improvement in hypersecretion accompany a reduction in hyperacidity, or, in other words, are both factors effected in the same manner by the medical treatment? A reference to Table II is instructive.

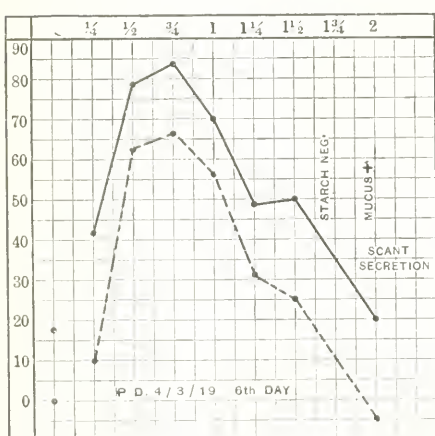


CHART XXII

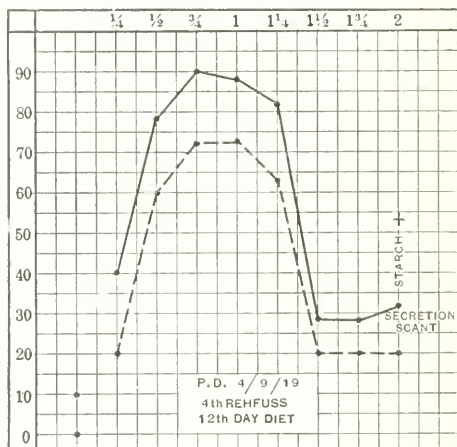


CHART XXIII

TABLE II.

Hyperacidity reduced; hypersecretion improved; clinical result: good, 6 cases; poor, 1 case.

Hyperacidity not reduced; hypersecretion not improved; clinical result: good, 8 cases; poor, 3 cases.

Hyperacidity not reduced; hypersecretion improved; clinical result: good, 2 cases. Total, 20 cases.

It is thus seen that in all but 2 cases, the last two in the table, both factors were identically influenced, either both being beneficially influenced or neither one affected for the better. The frequent coexistence of these two factors, and their similarity of behavior under treatment, suggests a close association between them.

As for the clinical results of treatment the same inconsistency is naturally seen in this group as in those in which only the effect on hyperacidity was considered. While in 11 cases, or 55 per cent., the treatment failed to affect the hypersecretion, yet 16 of the 20

cases, or 50 per cent., were discharged from the hospital clinically much improved and actually free of symptoms.

EFFECT OF MEDICAL TREATMENT ON GASTRIC MOTILITY. What is the result of our medical efforts upon delayed emptying of the stomach and persistent food residue?

Before proceeding directly to a critical review of the cases let us consider for a moment, as a preliminary, the question, "Is the fractional test-meal a good medium by which to judge the motility of the stomach?" There has been much discussion as to the relative merits of the roentgenological method for demonstrating delayed motility, and, on the other hand, of chemical methods for demonstrating postponed emptying. Both methods have undoubted value, and either method in the hands of a competent technician and observer, is beyond question, a reliable index of motility.

The fractional test-meal by allowing observations at such short intervals as a quarter of an hour seems to have the advantage over both other methods, these latter being limited to a single observation at the termination of a stated interval. With the fractional method one can state within a few minutes just when the last remnant of food has passed the pylorus. In every instance in which a six-hour residue was reported by roentgen-ray methods a chemical delayed motility was also evident with the Rehfuß method. On the other hand innumerable instances are met with in which slighter grades of delayed emptying are evident by this chemical method, which evade entirely the roentgenologist.

Using 500 c.c. of thick oatmeal gruel as a test breakfast, normal motility with the fractional method may be regarded as one and three quarters to two hours; in cases with moderate degrees of atony up to two and a quarter hours.

In this series of 34 cases of ulcer, or ulcer suspects, there were 13 instances of delayed motility, using the fraction test as a criterion. The time of emptying varied from two and a quarter hours to a maximum time of three and a half to four hours. It is in this field that the optimum effect of medical treatment was obvious.

The following two charts illustrate the improvement in motility which resulted in a case in which the diagnosis of penetrating ulcer of the lesser curvature was radiographically demonstrated. Chart XXIV is the curve taken upon admission to the hospital (service of Dr. E. Libman). Note that after three hours the iodine test for starch (oatmeal gruel) was still ++. After twenty-six days of treatment (Chart XXV) shows emptying time reduced to one and a half hours. This result is striking.

Or, another case, one of probable gastric ulcer; symptoms one and a half years in duration; periodic remitting attacks of heartburn and eructations and loss of weight. Chart XXVI is the curve on admission (service of Dr. E. Libman). The note on the chart reads "three and a quarter hours p. c., starch ++." Chart XXVII is the

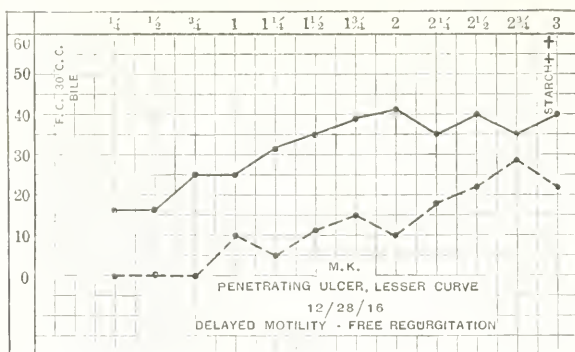


CHART XXIV

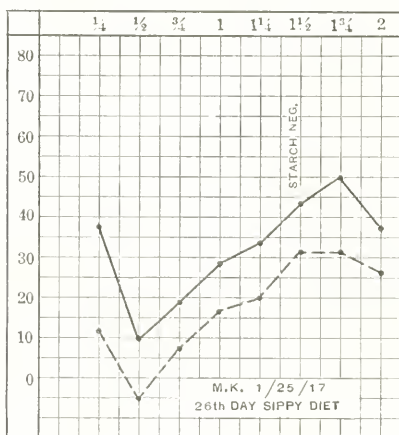


CHART XXV

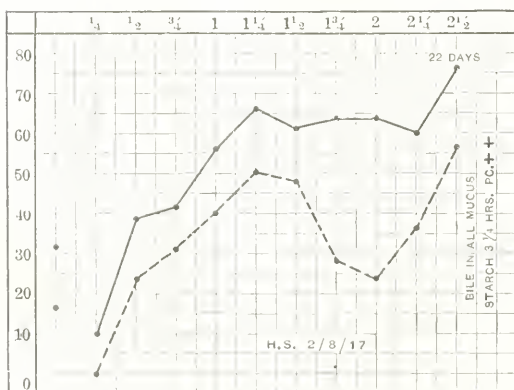


CHART XXVI

curve of the same case after six days of strict dieting; after two and a quarter hours the stomach has already evacuated the last traces of starch.

The preceding 2 cases are undoubtedly examples of delayed motility due to pylorospasm, for it is hardly conceivable that a real organic stenosis would have resolved in so short a period as six days, as obtained in the second of these 2 cases.

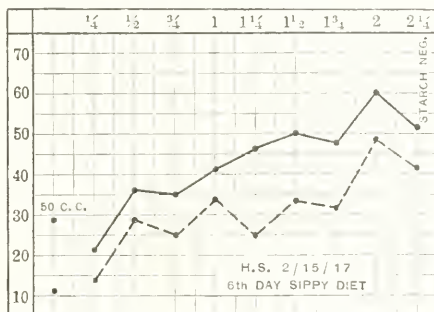


CHART XXVII

The following charts demonstrate the results of medical treatment in a case of organic stenosis due to pyloric ulcer. The patient, a man, aged fifty-four years, had been under my observation for about

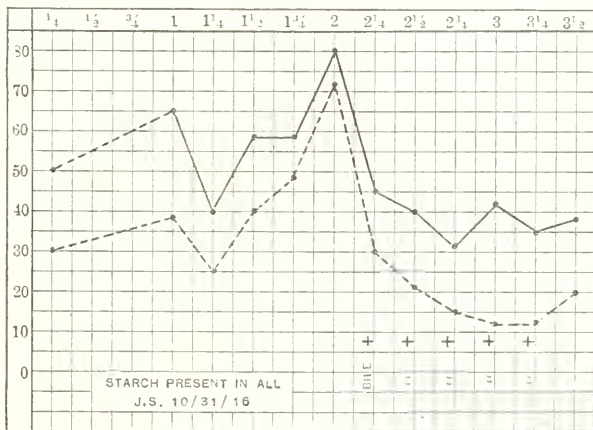


CHART XXVIII

two years. He had residual vomiting, periodic pain and loss of weight; his Ewald test breakfast showed high acidity, sarcine, yeast and marked food stasis. Repeated radiographic examinations failed to show a defect or suspicion of carcinoma, though confirming the delay in evacuation. Chart XXVIII is the acid curve upon

admission (service of Dr. E. Libman). At the end of three and a half hours starch was still present in all the specimens withdrawn. Chart XXIX is the curve on the ninth day of treatment. After three hours starch is still present in all tubes. Chart XXX is the curve on the fifteenth day of modified Sippy diet. Starch is present as a trace after two and three quarter hours, and is absent after three hours. It is also noted that the acid curve now falls to normal when the stomach becomes empty.

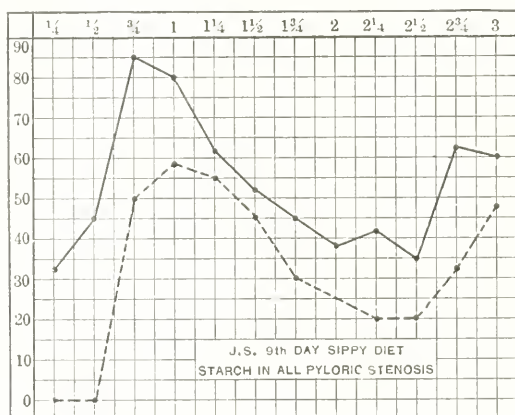


CHART XXIX

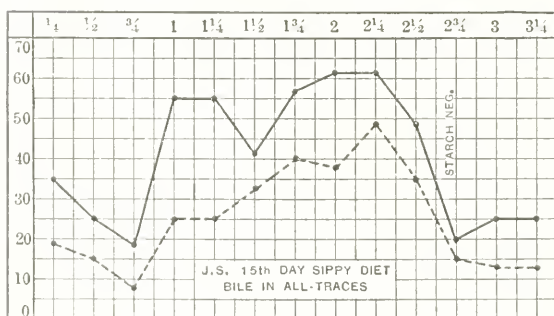


CHART XXX

In all but two of the cases of the series emptying time was definitely, in many of them markedly, shortened, a proportion of 85.4 per cent. Still more striking is the fact that clinical improvement as noted ran quite parallel with the reported improvement in motility. All of the 11 cases in which improved motility was accomplished were discharged free of symptoms, while the 2 cases in which the delay in motility resisted our efforts were discharged unrelieved of subjective symptoms.

A reduction of acidity did not always accompany an improvement in the motility. Thus of the 11 cases with improved emptying time, in only 3 was hyperacidity reduced, while in the remaining 5 the high acid curve persisted. In spite of the persistent acidity all of these cases were discharged free of symptoms.

Hypersecretion was noted 6 times in association with delayed emptying. In 4 of these 6 instances it was not relieved by the treatment; in these cases, though, the hypersecretion persisted, the pyloric stenosis or pylorospasm was relieved and the patient was discharged free of symptoms.

The following is a tabulation of the results of motility test which followed treatment and the day upon which the test was taken:

TABLE III.

Motility before treatment.		After treatment.	
Case 12	2 $\frac{1}{4}$ hours	1 $\frac{1}{4}$ hours	(12th day)
16	3 "	2 $\frac{1}{4}$ "	(6th day)
17	2 $\frac{3}{4}$ "	*2 $\frac{3}{4}$ "	(12th day)
21	3 $\frac{1}{4}$ "	3 "	(9th day)
		2 $\frac{3}{4}$ "	(15th day)
23	3 $\frac{1}{2}$ "	2 $\frac{1}{4}$ "	(7th day)
		1 $\frac{1}{2}$ "	(10th day)
		1 $\frac{3}{4}$ "	(12th day)
24	3 "	2 $\frac{1}{2}$ "	(3d day)
		2 $\frac{1}{2}$ "	(8th day)
27	2 $\frac{1}{2}$ "	2 $\frac{1}{4}$ "	(6th day)
28	2 $\frac{1}{2}$ "	*2 $\frac{3}{4}$ "	(3d day)
		2 $\frac{3}{4}$ "	(12th day)
30	2 $\frac{1}{2}$ "	1 $\frac{1}{4}$ "	(10th day)
34	4 "	1 $\frac{1}{2}$ "	(26th day)

* No improvement.

DISCUSSION. Having studied in detail the effect of restricted diet and rest in bed upon each of three factors which show deviation from the normal, let us try to evaluate the relative importance of the change which takes place in each of them. Let us attempt to estimate the relationship between clinical relief from symptoms (cure?) and physiological or chemical benefit.

Does medical treatment reduce the hyperacidity of ulcer, and if so, is this relief responsible for the clinical improvement?

Does restricted diet cause the disappearance of hypersecretion, and if it does, is this the factor that relieves the symptoms?

Finally, can delayed motility in the presence of ulcer be relieved by the feeding of small quantities of food often repeated? And if so, is this the factor that brings about apparent cure of symptoms? We will discuss these factors individually and collectively, recapitulating the findings in the body of the paper.

Medical treatment resulted in a net reduction of acidity in 13 out of a series of 34 cases (38 per cent.). If we wish to consider only those cases with definite hyperchlorhydria, omitting all cases with iso- or hyposecretory curves, the percentage of net lowering of acidity

is still lower (30.3 per cent.). Of these 13 cases chemically benefited 12, or 92 per cent., were discharged free of symptoms. Loose reasoning might lead one to see a relationship of cause and effect in these figures. But if we analyze those cases in which treatment failed to invoke chemical relief, and these comprise the larger proportion, we find, despite this fact, clinical relief in 13, or 62 per cent., of them. In other words, of 25 cases discharged from the hospital free of symptoms and apparently well, 13, nearly one-half, retained the same height and type of acidity as on admission. If clinical cure depended upon relief from hyperacidity then the optimum result should be in this class of cases. Almost 80 per cent. of the cases with hyperchlorhydria left the hospital clinically relieved, yet only 30.3 per cent. of these showed chemical relief from the excessive acid production.

We can draw two inferences from these figures: (1) Only a small percentage of ulcer cases react to medical treatment by showing a reduction of acid produced during digestion (38 per cent.); (2) clinical improvement can take place independently of whether the hyperacidity is relieved or whether the case remains acid-fast.

As regards hypersecretion a similar conclusion is soon arrived at. Twenty cases in the series showed hypersecretion; in 9 cases, or 45 per cent., medical treatment caused the disappearance of this abnormal factor, in the other 11, or 55 per cent. of the cases, medical treatment failed to alter the hypersecretion. Yet 80 per cent. of these cases left the hospital apparently well. Exactly 50 per cent. of the clinically cured cases still retained hypersecretion upon discharge from the hospital, and yet subjectively the pyrosis, heartburn and pain had disappeared.

From these figures we can again draw two conclusions: (1) Medical treatment, consisting of restricted diet and rest in bed, causes the cessation of hypersecretion in 45 per cent. of the cases, a fair proportion; (2) clinical improvement takes place as often in cases with persistent hypersecretion as in those relieved of their excessive flow of gastric juice, and is apparently not dependent upon it.

Finally, we shall discuss the relationship between improved gastric motility and clinical relief. There were 13 cases of delayed motility; in 11, or 85.4 per cent., medical treatment succeeded in alleviating this symptom and reducing the emptying time to normal. All of these 11 cases were in addition freed of subjective complaints. Two cases resisted treatment (motility unimproved), and they were discharged clinically unrelieved.

There are no instances of clinical cure that could be solely attributed to reduced acid secretion when delayed motility was present as a complicating factor. Unless relief is had from the pylorospasm we fail to note the disappearance of subjective symptoms. By stating that relief of pylorospasm results in clinical cure and is probably the cause for amelioration of symptoms we have only answered

part of the question. Most of the cases in this series were not complicated by delayed motility; they were cases with hyperacidity and hypersecretion but normal motility. We have tended throughout this study to discredit the idea that clinical relief is built upon a reduction of the hyperacidity or hypersecretion and can and does take place independent of chemical change.

Then to what change in the physiology or pathology of the stomach can one attribute the relief from symptoms in cases not complicated by pylorospasm? No data in this study throws any light on this question. The answer must be sought and will probably be found in the radiographic studies of Ginsberg, Tumpausky and Hamburger,¹⁰ Carlson,¹¹ Hardt¹² and others.

These authors have demonstrated the close relationship between subjective pain and exaggerated peristalsis or hunger contractions. It is quite likely that restricted diet and bed rest have a quieting influence upon gastric contractions, diminishing the amplitude and violence of these contractions. Reduction of acidity and secretion may or may not accompany the reduced tonus of the stomach.

The present study has demonstrated that in a fair proportion of the cases medical treatment caused reduction of hyperacidity and of hypersecretion. To what can be attributed the failure to effect this change in a far larger percentage? The answer probably lies in the fact that the marked restriction of food intake is not maintained for a long enough period. Almost all schedules of "ulcer diet" increase the number and amounts of food rapidly, particularly during the second week. In fact, Lenhartz already introduces meat on the tenth day. It is a common observation that hospital patients complain bitterly of being starved in the early days of dieting, yet it is just at this period that they report the disappearance of their annoying subjective symptoms. The end of the second week, which usually marks the period of increased alimentation, is a common date for reappearance of symptoms of pain and heartburn. It has further been shown that it takes up to the sixth to the tenth day for the acid secretion to show beneficial result, as evidenced in a lowering of the curve. The earliest effect of the marked food restriction is probably diminished tonus and contractions and increased rest to the stomach walls. The later effect is a fall of acidity and secretion. The full beneficial result, particularly on the hydrochloric acid production, is probably defeated by a too early return to a more liberal diet. The introduction of meat during the second or third week is harmful; meat-free diet should be continued for weeks or even months.

It is probable, too, that a diet based in its earlier stages on milk alone, rather than on milk and eggs as in the Lenhartz diet is to be

¹⁰ Jour. Am. Med. Assn., 1916, lxxvii, 990.

¹¹ Am. Jour. Physiol., 1917, xlv, 81.

¹² Jour. Am. Med. Assn., 1918, lxx, 837.

preferred. The amount of secretion called forth in the digestion of a milk-egg diet is far greater and the emptying time is much longer for a milk-egg mixture than for a milk meal, or certainly for a cereal meal. Personally, I would favor rather a greater liberality and earlier introduction of cereals and more restraint in the use of eggs.

It has been demonstrated in a previous paper by the author¹³ that antacids should be used often and in small doses, lest they in themselves increase or stimulate the acid cells to production. Nor can the influence of the psychological factor be overlooked. Mental contentment during a course of treatment is essential. A noisy hospital ward; the bad example of a bed-neighbor who is a neurotic and constantly complaining of the food, the treatment and his symptoms; mental disturbance over economic conditions at home, are all influences that tend to cause persistence of secretory and motor abnormalities and deprive the patient of the full benefit of his rest in bed and dietary cure. This principle applies as well to the ulcer cases as it more evidently does to the cases of functional secretory disturbances or neurosis. A patient who is unhappy during his treatment is unlikely to get well.

One cannot overlook the physical difficulties of treating many cases by "ulcer diet" in a busy hospital ward. The war intensified these difficulties many times by creating a shortage of nurses. It is not an easy matter for a limited number of ward nurses to serve milk every hour, give antacid medication on the alternating half-hours and look after the general wants of the patients in addition. Cereal which has been delayed in transit and becomes cold is tasteless and to many patients disagreeable to eat. I fear that many of the failures to obtain better results are due to the physical inability of even the best hospital staff to live up to the details and the schedule of these time and attention-consuming dietary regimens.

Segregation of cases and special nursing facilities would solve many of these difficulties. This probably explains why the results in private practice are far better and more permanent than those in the hospital public service.

Cases that fail to show clinical and chemical improvement are of two kinds: those with advanced indurated ulcers which are resistant to treatment and those with marked neurosis. The first class can be reduced in number by more persistent and more protracted treatment. The second group requires the expert care of a neurologist, often of a psychoanalyst. Mistakes in diagnosis undoubtedly form a third group of not inconsiderable proportion. The beneficial effects of medical treatment are seen in those cases of hyperacidity, hypersecretion and pylorospasm accompanying latent cholelithiasis or chronic appendicitis, as well as in ulcer cases or functional

¹³ Crohn; Jour. Am. Med. Assn., 1918, clv, 801.

secretory disturbances. This remark applies to immediate results rather than to permanent benefits.

It is to be regretted that the cases in this series could not be observed for a sufficiently long period to determine the durability of the result and to determine whether a relation existed between improved physiological function and permanent cure or relief.

There is a large field for research still open along these lines. Much remains to be learned regarding the physiology and pathology of the stomach during and after medical treatment. It is only by close study and observation that we will learn to account for our failures and learn to recognize the factors that contribute to the clinical cure of these patients.

CLINICAL EXPERIENCE WITH SAHLI'S SPHYGMOBOLOMETER.¹

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WHEN this study was first begun nearly ten years ago it was with the purpose of applying a method of studying the circulatory efficiency of chronic diseases in measurable units, and so, of estimating the effect of drugs, of exercise, of rest, of food and of other extramedicinal measures, in order to prescribe any or all of them sufficiently accurately to promote the most rapid recovery, to continue the greatest efficiency and to avoid overloading the circulation.

Up to then no functional tests of the efficiency of the circulation, even as satisfactory as the modern functional tests of renal elimination, had been devised, especially for chronic invalids with damaged hearts, vessels and kidneys. The method of *Sphygmobolometry*, which the Swiss clinician founded upon the dynamics rather than upon the statics of the circulation, certainly promised much; and the later simplified and more accurate method of *Volume bolometry*, even more.

I purposely limited my two previous papers² of this series,

¹ From Memorial Laboratory and Clinic, Cottage Hospital, Santa Barbara, California.

² Potter, N. B.: Sahli's Pocket Sphygmobolometer; Demonstrated at a meeting of the Medical Section of the New York Academy of Medicine, November 19, 1912. Potter, N. B.: Sahli's Volume Sphygmobolometer; A Recent Improvement over the older Pressure Sphygmobolometer; AM. JOUR. MED. SC., October, 1918, No. 4, clvi.

practically to little more than a description of the instruments, awaiting a clinical contribution long expected from the Berne Clinic. Its place, however, has been usurped by highly technical articles which have from time to time appeared in various German journals of internal medicine, largely theoretical disputes between the erudite Director and one of his former pupils, Christen. Most modern clinicians, surfeited by carefully studied and prepared methods of exactitude, and instruments of precision, have acquired the habit of following lines of least resistance, avoiding polemic discussions, and largely utilizing only the exact, and the, so to speak, ready-made. This natural and mentally lazy tendency, and the incidence of the long war have unfortunately prevented, at most clinics, both here and abroad, the recognition as well as the application of this new conception and method of studying the circulation.

A THIRD INSTRUMENT. The writer's modification of the Volume Bolometer. After several years' experience with both of these

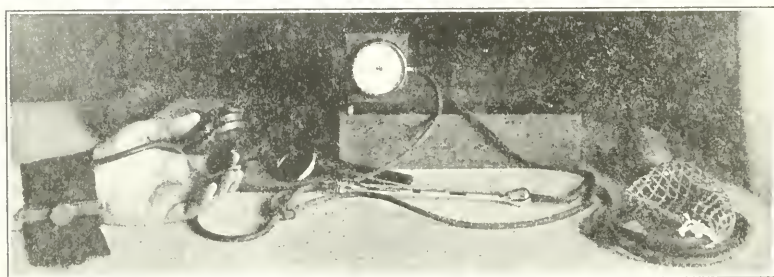


FIG. 1

instruments, the writer became convinced that a more compact and portable instrument, and one less liable to break in transportation could be made; in other words, one so conveniently constructed as to require no setting up and taking down each time it was used at a different place, and quite as serviceable for house-to-house practice as such American Sphygmomanometers as the Tycos and Sanborn instruments. The writer has, therefore, devised and had constructed, with the aid of one of his assistants, Dr. R. R. Newell, the simple modification exhibited in Fig. 1. It requires no further description than this illustration to make its advantages apparent. It enables the observer to take the blood-pressure immediately before or after he makes the Sphygmobolometer estimation, with the same spring manometer. It is so combined as to be very compact, portable and non-breakable, and can be applied, taken off, repacked in a box $10 \times 4\frac{1}{2} \times 2\frac{1}{2}$ inches and slipped into the observer's bag with the greatest ease and despatch. In this respect the writer feels

he owes a distinct apology to the distinguished inventor, knowing the latter's well founded objections to the substitution of a spring for a mercury manometer. If any reasonable demand for such a combined instrument occurs, Dr. Sanborn has been kind enough to offer to supply it.

A few paragraphs will suffice to dispose of the pressure bolometer, and perhaps this can best be done by quoting from one of Professor Sahli's personal communications. From our own point of view it is only necessary to inform the reader that we also had entirely substituted the latter for the former instrument, that some of the suggestions he so kindly gave us we find very helpful for the volume bolometer, as we did for the pressure instrument. We have made something more than a thousand observations with the pressure and two thousand with the volume bolometer, from which the data, tables and charts presented below have been collected. In the following charts and tables we have indicated observations which were made by the original pressure instrument; also those obtained with use of the volume bolometer by our group of workers in New York and at the Memorial Laboratory and Clinic, Santa Barbara, California. My reasons for this are, that although in the main our observations have proved uniform with both instruments and with both groups of workers, there has been, almost from the start, great difficulty and delay in obtaining duplicate instruments, fresh supply of rubber tubing, pelottes, etc., and the substitutes and crude repairs have been relatively so unsatisfactory, especially since the war, that some discrepancy in our figures has unavoidably occurred.

We may here quote from Sahli's personal communication:

"In regard to the comparison between the estimation of the 'Pulse Work' with Volume and Pressure instruments which you have again requested, I can add nothing to what I have already published. This proves that the two methods reveal approximately equivalent values for the pulse work; that the principle for both is correct and that if we employ sufficient care in the optimal adjustment of the cuff, and with the pressure instrument this detail is often tedious and difficult, we can obtain values for 'Pulse Work' which are clinically useful. Since these values in the figures published do not deviate much, one from the other, and since the optimal pressure with the proper application of the cuff does not usually vary markedly in the two methods, the pulse volume (considering the optimal pressures as equivalent) may be readily reckoned in pressure bolometry from the values for the 'pulse work.' 'Pulse Work' is equal to the 'Pulse Volume' times 'Optimal Pressure' times sp. gr. of hg. Perhaps, for the purpose of this communication, this last (sp. gr. hg.) has no significance, so that I have disregarded it.

"As far as your own estimated figures are concerned (a series of observations made upon some of my patients with the estimations and equations worked out in detail which I submitted to Prof. Sahli for criticism) your method of reckoning is correct. I have taken the pains to go over them all very carefully, and have found only quite unessential variations, probably due to the technique of your figuring."

For the reader who is interested the later bibliography upon the subject of Sphygmobolometry is appended below. There are, however, in addition to the Professor's own communication, several papers of considerable interest. The first,³ from the Berne Clinic itself, concerns the combination of Sphygmobolometry and Jaquet's Sphygmography, for the details of which the reader is referred to the original article. The second,⁴ from Naegeli's Clinic at Tübingen, in which a number of observations are reported. Many of them are made with the original pressure instrument, chiefly upon normal individuals, upon a series of long-distance runners before and after a test run, and upon oarsmen before and after a race. The majority showed a sharp rise in the work of the pulse at the end of the exercise, which he considers a normal response. A few showed no effect, or a diminution in the work, which he regards as evidence of a weakened circulatory reaction, and which he explains in one case by a drinking bout the night before, and in another by the remains of an old myocardial lesion.

The author, Hartman, tested four students before and after a drinking bout, with the uniform result of an increase in pulse-rate and drop in the pulse work. Again, he made numerous tests upon a few students after an excessive consumption of coffee, tea and nicotin, as well as many times after a moderately excessive ingestion of alcohol, practically always resulting in a considerable increase in the bolometric values. He concedes the difficulty of formulating a definitely normal value, but shows in four individuals how little the pulse work varies in one and the same individual, over a period of from five to six months. Upon the basis of measurements on fifty students, he formulates the normal between 6 and 14 g.cm. In older and stronger individuals the upper normal limit may reach as high as 15, and in younger males and in females, fall as low as $4\frac{1}{2}$. One of his experiments with twenty students shows how wide a variation may exist in the values obtained from the same individual, without any pathologic reason therefor. During the course of the spring season two measurements show approximately constant values, but the third time upon an extremely relaxing and

³ Sahli: Ueber die Verwendung moderner Sphygmographen, speziell des Jaquet'schen, zu sphygmobolometrischen Untersuchungen. Die Sphygmobolographie eine klinische methode, *Corr.-Bl. f. Schw. Aerzte*, 1911, Nr. 16.

⁴ Hartman, Carl: Untersuchungen mit dem neuen Sphygmobolometer nach Sahli, *Deutsch. Arch. f. klin. Med.*, 1915, Bd. 117.

oppressingly hot summer evening, sixteen out of the twenty showed an increase of from 1 to 2.5 g.cm. Most of those examined, including myself, very few of whom were physicians, felt the excessive filling of the arm veins. Upon a few pathological individuals before, during and after the use of digitalis, caffeine, etc., his records, charts and the description of his work show careful, accurate observation, and are closely in accord with our own results.

He concludes as follows:

1. In perfectly healthy individuals the bolometer values vary excessively—from 6 to 13 or 14 g.cm.

2. The values in a single individual, however, remain remarkably constant over months.

3. Diurnal, physiological conditions, however, lead to not inconsiderable variations, which exhibit themselves characteristically with the bolometer conditions, even when no deviation can be shown by any other method. Therefore the analysis of Sphygmobolometric measurements, make our knowledge of physiologic, as well as pathologic, alterations considerably more profound than delicate.

4. The study of a continuous curve upon one individual, charted out over a considerable period of time, is especially valuable.

5. Physiological efforts, such as occur in sports, like long-distance running and rowing, will, if the test calls forth a moderate effort, produce a moderate increase in the bolometric value; a greater effort will produce a corresponding rise, and as the strength wanes, so too, does the bolometric value decrease.

6. The consumption of alcohol, tea, or nicotin exhibits similar alterations.

7. In the study of the capacity of the cardiovascular apparatus in pathological cases one obtains valuable conclusions from the bolometer.

8. Digitalis therapy gives successful results in the elevation of the bolometric values. When such decrease, so too, does the therapeutic effect of the drug.

9. Support in prognostic conclusions is afforded by this method, when all other methods fail.

Another important article is from the Clinic of the master himself.⁵ Regarding this article Sahli wrote me as follows:

"It was not until Dr. Dubois had almost completed his thesis upon pressure bolometry that volume bolometry originated, so he was unable to utilize it. It was soon evident that most of his values were lower than the corresponding volume bolometric values."

"Unable to oversee his work minutely I cannot be sure that each estimation was made with an optimal application of the cuff; nevertheless his clinical observations are quite serviceable if limited to the comparison of one and the same individual at different times, since

⁵ Dubois: Sphygmobolometrische Untersuchungen bei Gesunden und Kranken, *Deutsch. Arch. f. klin. Med.*, 1916, Bd. 120.

the chief defect depends upon the anatomical configuration of the wrist-joint region, and so in the estimations upon the same person the figures vary but slightly. Although he had estimated a large series of normal values, at my insistence they were not included in his publication because my assistant, da Cunha, will establish these for volume bolometry alone and later on will publish them. I do not want to cause confusion by presenting two sets of normal values."

The article of da Cunha⁶ to which Sahli refers, gives us normal values for the volume of the pulse and for the pulse work, which, despite the inherent difficulties of the method and its interpretation, are of no little utility in the estimation of pathologic cases. Da Cunha's summary follows:

Statistics for normal males, age sixteen to forty-nine years:

Radial pulse volume: Maximum, 0.15 c.cm.; minimum, 0.05 c.cm.; average, 0.09 c.cm.

Radial pulse work: Maximum, 17.14 g.cm.; minimum, 6.12 g.cm.; average, 11.27 g.cm.

Minute's volume of radial pulse: Maximum, 11.2 c.cm.; minimum, 3.0 c.cm.; average, 6.81 c.cm.

Statistics for normal females, age sixteen to forty-nine years:

Radial pulse volume: Maximum, 0.11 c.cm.; minimum, 0.04 c.cm.; average, 0.07 c.cm.

Radial pulse work: Maximum, 17.95 g.cm.; minimum, 5.98 g.cm.; average, 10.19 g.cm.

Minute's volume: Maximum, 8.8 c.cm.; minimum, 2.4 c.cm.; average, 5.56 c.cm.

After a seven o'clock breakfast, taken in bed, the pulse-rate increases, but there is little variation in the volume and work of the individual pulse. Half an hour after a large midday meal the volume and work of the individual pulse, rise, whereas the pulse-rate remains stationary. Two hours after the midday meal the pulse volume resumes its original value. The pulse work likewise decreases, but not with the same regularity. It may return to its original value or it may fall slightly above or below it. The rate of the pulse is now lower than before the consumption of food.

Charts 13 and 14 illustrate my own observations on normal or approximately normal subjects before and after the noon meal.

On changing from a lying to a sitting posture there is an acceleration of the pulse, but in both pulse volume and pulse work there is a decrease so great that, despite the increase in pulse-rate, there is a distinct fall in the minute's volume and the minute's work.

My observations in regard to posture are illustrated by Chart 6.

Da Cunha's article shows that his work was done in the usual

⁶ da Cunha, D. Jose: Beiträge zur Beurteilung der Resultate der Sahli'schen Volumbolometrie nach Untersuchungen bei Gesunden, Corr.-Blatt f. Schweizer Aerzte, 1917, Nr. 46.

accurate fashion of the Berne Clinic. Most of his observations are quite in accord with our own. His illustrations are unusually simple, clear, and striking. This paper should be consulted by anybody planning to utilize the instrument and the method.

On account of the war, four of the more recent publications⁷ have been, and still are, inaccessible to the reader on this side of the water. However, Reinhart's very recent article⁸ reveals much of what is most essential. Reinhart regrets the extreme paucity of the literature.

Brösamlen entirely discards the method because of the influence exerted upon the values he obtained by varying vasomotor conditions. He denies that any conclusions of permanent value in regard to the cardiac-systole can thus be obtained. In his last communication Sahli replied to the above criticism, pointing out the incomplete and incorrect protocols upon which Brösamlen's conclusions were based; also his entire neglect of the pulse-rate, and failure to report the pulse volume in addition to the work. Individual variations of the caliber of the radial artery, as induced by the effect of heat and cold upon the arm, may of course have been responsible for considerable fluctuation in the pulse volume, and so too, may general vasomotor influences. Sahli believes, however, that, taking all factors, such as pulse-rate, into consideration, dependable values for the measure of the volume of the circulation can be obtained, unless there are gross vasomotor or anatomical abnormalities of the radial artery.

Reinhart, using the new sphygmovolumeter with great care as to application of the cuff, endeavored to determine, by simple experiments in which the volume of the heart-beat could be considered positive, whether a demonstrable increase or diminution of the systole would also be manifested in an increase or diminution of the sphygmovolumeter volume. Working with large and small hearts, on the theory that, aside from anomalies such as mitral insufficiency, a larger heart must be associated with a larger heart-beat volume, the author obtained results which conformed in every respect with the roentgen-ray findings. In 130 examinations made with the sphygmovolumeter on 30 normal individuals and 25 patients with valvular lesions, this author demonstrated the fact that the volume of the pulse diminishes as the patient changes from horizontal to

⁷ Brösamlen: Die Bedeutung der Pulsuntersuchung f. die Bemessung des Herzschlagvolumens, Deutsch. Arch. f. klin. Med., 1916, Bd. 119. Dubois: Sphygmobolometrische Untersuchungen bei Gesunden und Kranken, Deutsch. Arch. f. klin. Med., 1916, Bd. 120. Müller, O., und Brösamlen: Ueber die Eignung der Sphygmobolometrie resp. Sphygmovolumetrie zur Bemessung der Systolegrösse resp. des Minutenvolumens, Deutsch. Arch. f. klin. Med., 1917, Bd. 124. Sahli, H.: Ueber die richtige Beurteilung der Volumbolometer und die Art ihrer Klinischen Verwendung zugleich Erweiterung auf den Aufsatz von Dr. Brösamlen, Deutsch. Arch. f. klin. Med., 1917, Bd. 122.

⁸ Reinhart, A.: Ueber die Eignung der Sphygmovolumetrie zur Bemessung der Systolengrösse, Deutsch. Arch. f. klin. Med., 1918, vol. cxxvii.

the upright position, corresponding directly with the diminished size of the heart in the upright position. This decrease averaged 20 per cent. to 30 per cent., but in individual cases amounted to 45 per cent. to 50 per cent. in special patients. In these experiments, as the volume decreases the pulse-frequency rises, thereby partly, but not entirely, compensating in minute's volume for the reduction in size of the single pulse. Corresponding with the diminution of the volume, the maximal pressure also drops as a rule 10 to 15 mm. of mercury.

In a series of experiments with the Valsalva test, Reinhart demonstrated a diminution of the sphygmovolumetric pulse volume conforming with the decrease of heart-beat volume demonstrated by the roentgen ray. This diminution of the pulse volume points to a diminution of the heart-beat volume, and, *vice versa*, a diminution of the heart-beat volume points to a diminution of the pulse volume.

In a third series of experiments, it was demonstrated that fluctuations in the pulse volume occur under forcible inspiration and expiration. In *pulsus paradoxus* and respiratory arrhythmia the smaller systoles at the beginning of the inspiration were associated with smaller pulse volumes. Sixty cases without respiratory arrhythmia showed, with few exceptions, a decrease in the pulse volume at the beginning of inspiration, corresponding to the theoretical decrease in the systole on inspiration.

In his fourth series of experiments the author found that in changes of frequency of cardiac contractions, induced by stimulation or paralysis of the vagus nerve, by means of pressure and of atropin respectively, the high-frequency contractions were accompanied by smaller pulse volumes than were the low-frequency contractions.

Finally, it was shown from pathological cases that pulse volume is dependent on heart-beat volume; as in cases of compensatory disturbances with a small systole and in pulmonary edema with failure of the left ventricle, where a distinct diminution is noted in the volume of the pulse, pulse volume again increasing under improvement of the circulation.

Reinhart, then, in his carefully executed experiments, establishes that the pulse volume as measured by sphygmovolumetry is directly dependent on the size of the systole; hence the pulse volume registered by the sphygmovolumeter affords a method for determining the size of the systole. These experiments seem positively to refute the violent attack made upon sphygmovolumetry by O. Müller and Brösamlen.

What is this dynamic measurement? Is it of clinical value, sufficient to justify the amount of training, patience and time essential to its employment? It was not until some years after *Sphygmomanometry* had been demonstrated to be an essential addition to any physical examination, that it was proved beyond peradventure

that even an expert could not estimate blood-pressure with any degree of accuracy by ordinary finger palpation of the artery alone, although this had formerly been supposed possible. For centuries every physician has been palpating the pulse in order to be able to determine by the pressure of his finger an approximate value of *pulse volume* and indirectly, although generally unwittingly, a rough measure of *pulse work*. Without discussing the value of such dynamic pulse conceptions, or even whether they do actually furnish determinations of the same relative value as for the heart itself, it may be stated positively here that none of us who have been working with these instruments have the slightest doubt that the ordinary finger palpation of the pulse is incapable of furnishing even a skilled observer much if any more dependable results in this dynamic measurement than, unaided by an instrument of precision, he is able to obtain of blood-pressure with its static measurement. If we can prove, therefore, that these dynamic measurements are of clinical value, either in diagnosis, prognosis, or treatment; that they can be reasonably accurately determined by Sahli's latest instrument, the so-called *Volume bolometer*; that the essential skill and experience for its use can be obtained by any competent clinician or laboratory technician within a brief period; and that the procedure requires but a moderate amount of time for each estimation; we shall then have definitely demonstrated that the fecund Swiss clinician has added another and a most valuable method for accurately studying the circulation, and one from an entirely new viewpoint. The older method *Sphygmobolometry* or *Pressure bolometry* has been entirely discarded by its originator at his Clinic at Berne and permanently supplanted by *Volume bolometry*. Our observations, however, with the earlier method may be utilized in a tabular and statistical form to prove that even with this inferior, much less accurate, and much more time-consuming method, quite dependable results were obtained by my assistants after but a few weeks' training and experience.⁹

With the aforesaid purpose in view, we have, therefore, made no special or definite effort to establish a table of normals, based upon either decade, sex, size or weight; or to more than point out such gross differences in both *pulse work* and *pulse volume* as are well exhibited by such cases as an emaciated, weakened, starving diabetic, well-compensated aortic insufficiency, essential high blood-pressure, or an enormously hypertrophied heart from long-standing chronic nephritis. Such differences will be frequently noted in the

⁹ I acknowledge with much appreciation and thanks the devotion, patience and industry of Drs. Bradbury, Ordway, Brownlee, Ramurez and others who made these observations from which these tables and statistics were collected. Before their results were fairly uniform and trustworthy, each one of them required from three to eight weeks' practice, depending largely upon their previous experience with instruments of precision. Of course their observations were not utilized until they had developed this degree of skill.

figures below. After several years' experience I believe that this new method of studying the circulation will prove to be of essentially more value in comparing the daily figures furnished by a single case, or of the effects of various methods of treatment, medicinal or extra-medicinal in some one individual than in helping us to diagnose the disease in question or even to compare one patient with another by a single bolometric determination upon each. In the first place a number of determinations would always be necessary in order to

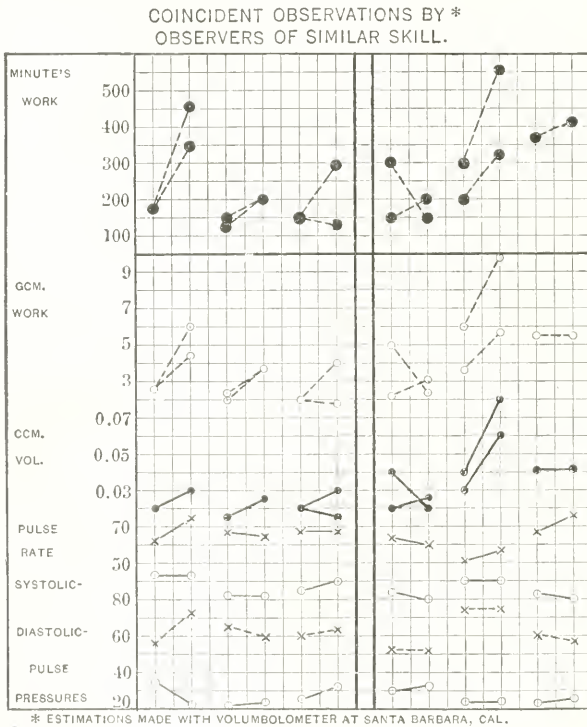
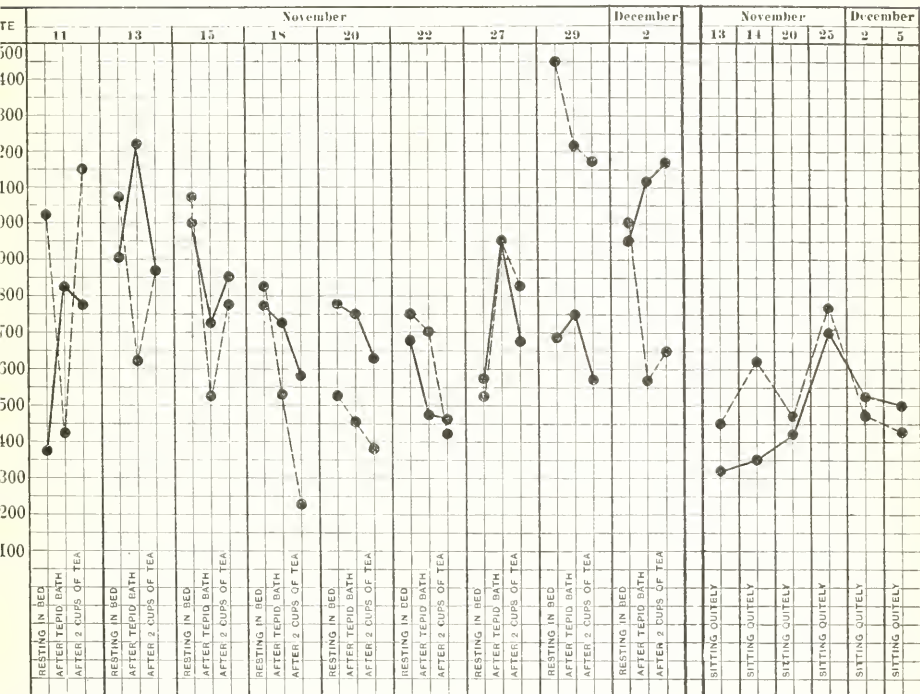


CHART I

arrive at an approximately uniform figure for this or that individual patient's normal. In the second place each patient's normal radius is relatively wide, especially so as compared with the border limits, and is influenced by many temporary, even momentary, emotional and other unavoidable causes. However, after what may be called the normal variations for an individual are once determined the effect of various causes when measured in *gram-centimeters of work*, or better still of *MINUTE WORK*, should prove of considerable clinical value.

ACCURACY. Chart 1 shows the results of coincident estimations on opposite wrists of the same individual by two observers of reasonably similar skill and experience. As will be seen in most instances, the agreement is striking. Where such wide discrepancies result as the last reading on Case 1, and the first reading on Case 2, it is generally because of the differences of the size and position of the radial artery, perhaps most often the latter; for in the many emaciated diabetic patients upon whom most of these tests were

CHART OF MINUTE'S WORK ON DIABETIC AND NORMAL TWO OBSERVERS OF DIFFERENT SKILL*



*ESTIMATIONS MADE WITH VOLUMBLOMETER AT SANTA BARBARA, CAL.

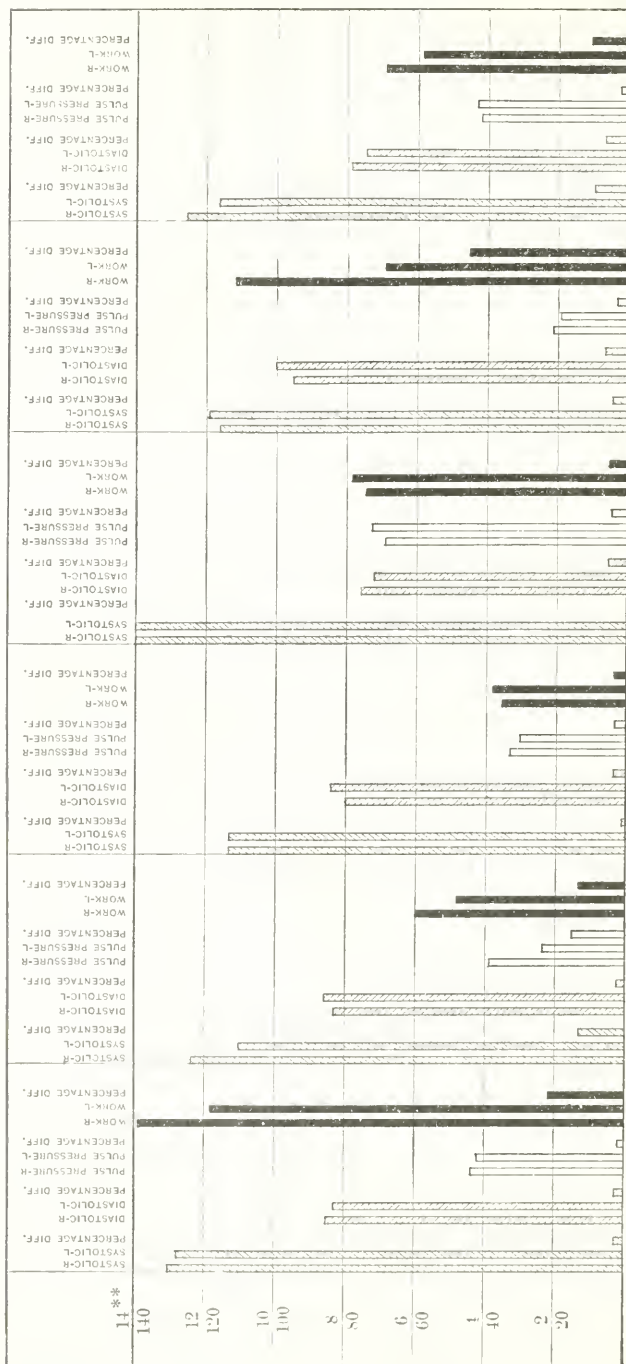
CHART 2

made, the difficulty of adjusting the wristlet properly is almost insurmountable, requiring infinite time, patience and frequent repetitions.

Chart 2 shows the variation between similar observations made by observers of markedly different skill and experience.

Chart 3 compares graphically the percentage of variations in the two wrists when the observations were made by the same worker under as nearly as possible identical conditions, the one immediately after the other, utilizing systolic, diastolic and pulse-pressure and

PERCENT OF VARIATION IN TWO ARMS.*
 BLOMETRIC AND BLOOD PRESSURE READINGS



* ESTIMATIONS MADE IN NEW YORK.
 ** NUMBERS ABOVE LINE REFER TO GCM. WORK, THOSE BELOW LINE REFER TO BLOOD PRESSURE.

CHART 3

work. Although the blood-pressure is ^umuch more in conformity, yet the difference is not striking.

Thus it may be concluded that there is scarcely less of accuracy or variation in this modern method *Volume bolometry* than in *Sphygmomanometry*.

TIME REQUIRED TO BECOME EXPERT. Prof. Sahli states ten minutes, but this time varies so greatly with the individual technician that it is difficult to obtain definite figures. My experience, however, with the many assistants who have so devotedly aided me in this study has led me to conclude that, like most other painstaking methods of precision with relatively delicate instruments, the whole affair is largely a matter of temperament, considerably a matter of training in similar methods, and no little dependent on the great quality of patience. From twenty-five to one hundred estimations usually fit a competent, well-trained technician to make dependable estimations.

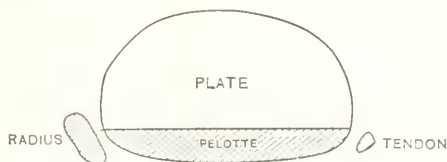


FIG. 2

TIME EXPENDED UPON EACH DETERMINATION. Each determination requires, according to the speed of the technician, and the type of patient, especially the position of his radial artery, upholstery of fat about the tendons, and configuration of his wrist, from two to three times that required to perform a systolic and diastolic blood-pressure determination by the usual auscultatory method with the Tycos or Sanborn instrument.

APPLICABILITY, CONVENIENCE AND ANNOYANCE TO THE PATIENT. Delirious patients with pneumonia, thrashing about continually, render such estimations extremely difficult, or impossible; but the ordinary quiet delirium of typhoid fever, or pneumonia, scarcely increased the difficulty of its application. The essential importance of a placid temperament in the observed as well as in the observer is self-evident. In Charts 13, 14, 15 and 16 any reader can readily select which of the observed individuals belong to this enviable category and which have an emotional, excitable, unstable nervous system. Variations in *Minute Work* represented by more than 100 per cent. have been observed to follow such slight nervous influences as the interruption of a telephone message. After all, it is wise to keep in mind that one essential feature of the greatest importance in the correct interpretation of incongruous results should first be attributed to the configuration of the wrist and to the

varying application of the cuff. In this respect, Prof. Sahli wrote me the following helpful suggestions:

"Great variations in the configuration of the tissues at the wrists of different individuals is responsible for one of the most telling difficulties in each application of the cuff for a proper optimal pressure. In one person the application is extremely easy, in another much patience and time are required on account of the way the plate is supported on one side by the styloid process of the radius and on the other by the tendon of the flexor carpi ulnaris, bridging over to a certain extent the pelotte in an excavation of the plate, thus:

"One frequently applies the plate *farther up* the arm because in bony and tendinous individuals it is impossible to succeed at the usual point of application, whereas, in addition to the separation of bone and tendon higher up, the better upholstered soft parts are also of assistance. Another help is sometimes afforded by *revolving the plate* along its long axis.

"The *throttled manometer* which I formerly employed to avoid a loss of energy, proved superfluous and I discarded it. It too may be responsible for mistakes in pressure values because *sometimes with the higher pressures it does not register correct values.*

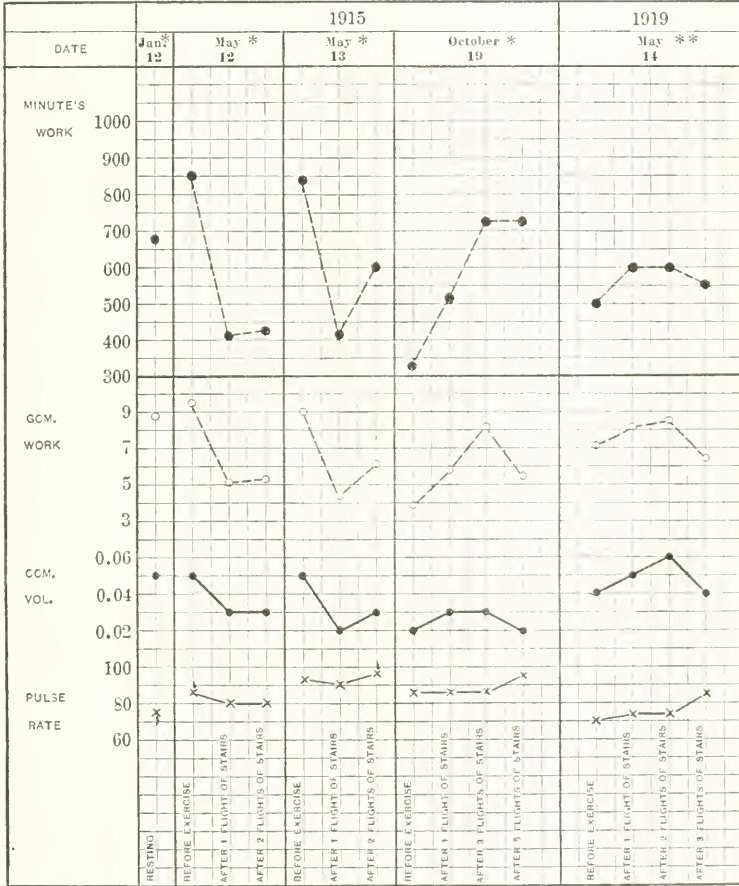
"The *glass connections*, too, must be of the same very small calibre. All these affect the multiplication factor, ϕ , which only applies to the caliber, the length of the conducting tubes and the air content of the system above mentioned. Though very impractical, leaden tubes would be preferable to rubber tubes in pressure bolometry.

"In pressure bolometry spontaneous relaxation of the cuff must be carefully avoided, for despite its very good application the vigorous pulsating force exerted, may gradually cause it to yield and even to become definitely distended. This change is much less liable to occur in volume bolometry because of the much less decided variations in pressure. As a result of such yielding there may arise materially incorrect (too small) pressure bolometric values.

"Certain possible errors may occur even in the reading. As you have noted yourself, they depend upon the effect of the variations in the respiration and of Traube's waves (periodic vascular contractions) continually dislocating the index and altering the size of the excursions. Hence, when the excursions are small much practice is needed to read them accurately, especially in pressure bolometry. So, too, the endpoint of the excursions is difficult to determine in the frequently lightning-like rapidity of the pulsations, because the retinal impressions are so transitory that one scarcely appreciates the index endpoint which persists near the latter so very brief an instant as to produce scarcely any color appreciation. This difficulty is all the more accentuated because the extremity of the index is not a straight cross line, but a sort of swollen meniscus

scarcely visible, as a result of the rapidity of the motion. The lower meniscus less bowed than the upper is, therefore, more easily read and gives frequently higher readings than the upper. The same difficulty occurs in both instruments, but is more significant in pressure bolometry where the absolute size of index is less. Since

PERMANENCY OF PULSE WORK



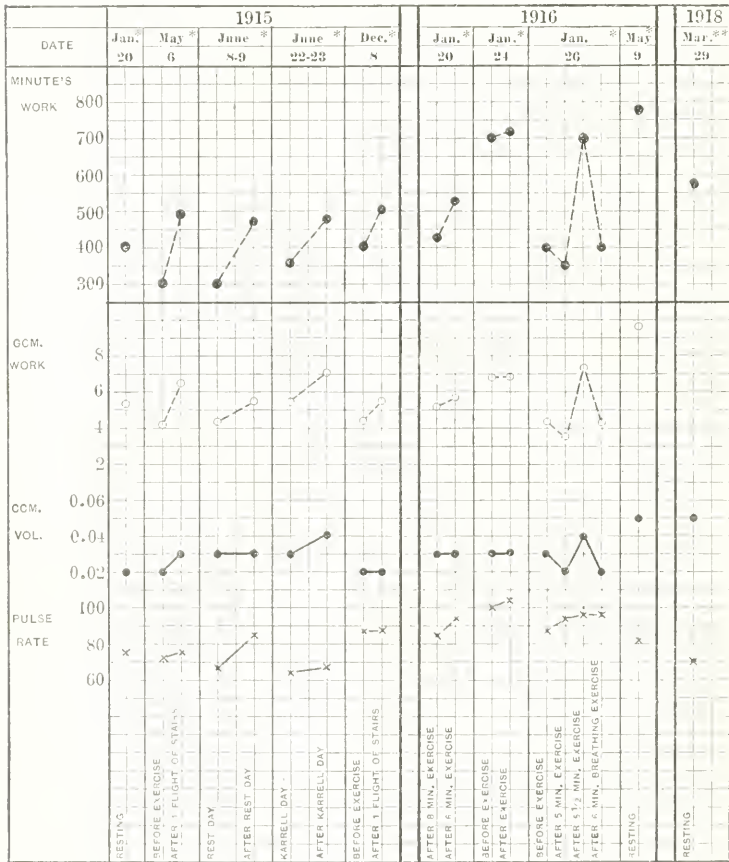
* ESTIMATIONS MADE IN NEW YORK
 ** ESTIMATIONS MADE IN SANTA BARBARA, CAL.

CHART 4

the difficulty is repeated at both the upper and the lower ends of the excursions, errors in reading of as much as 1 mm. may readily occur with rapid pulsation, and, e. g., at an optimal pressure of 10 cause variations of about 2 g.cm. I attempted to facilitate the readings in very rapid oscillations by employing a diminishing loop

and so reducing the rapidity of the retinal impression, but the experiment had the drawback of diminishing at the same time the absolute measure. Errors may also arise if the system is not perfectly tight, and unnoticed the pressure gradually falls during the observations and the reflux index movement resulting from the falling of the pressure is then superimposed with consequent too

PERMANENCY OF PULSE WORK



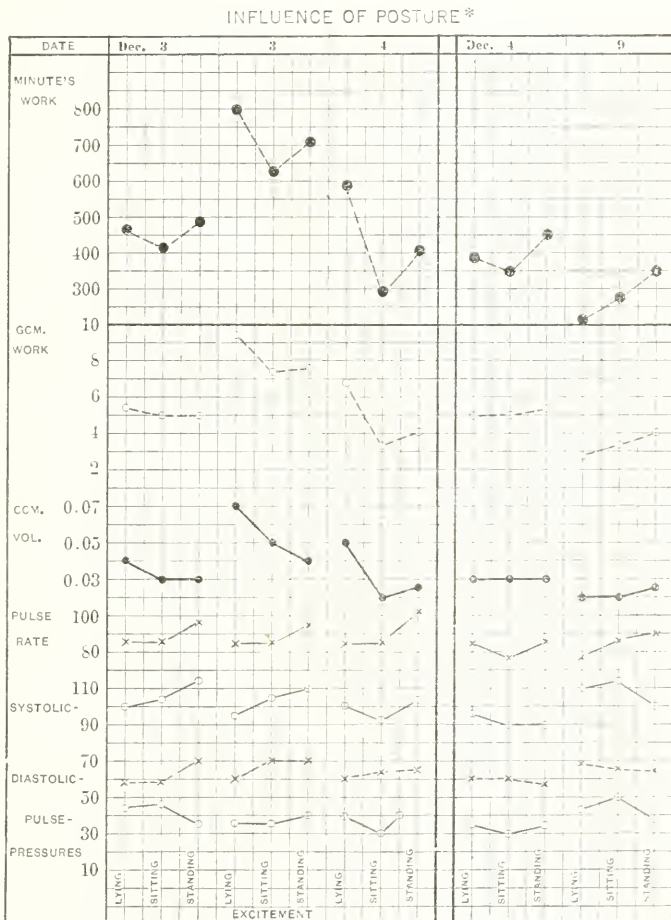
* ESTIMATIONS MADE IN NEW YORK
 ** ESTIMATIONS MADE IN SANTA BARBARA, CAL.

CHART 5

low values. In pressure bolometry this possibility of error is, on account of the smaller excursions, of greater significance than in volume bolometry. Besides, the optimal pressure frequently falls very rapidly without being noticed and too low values are thus read off.

"The most important cardinal points after all, are:

- Insufficient tension of cuff;
- Deficient rigidity of rubber tubing;
- Loosening of the cuff;
- Leaking in the system;
- Reading errors on account of the rapidity of excursion and the obscurity of the index meniscus with the rapid movement.



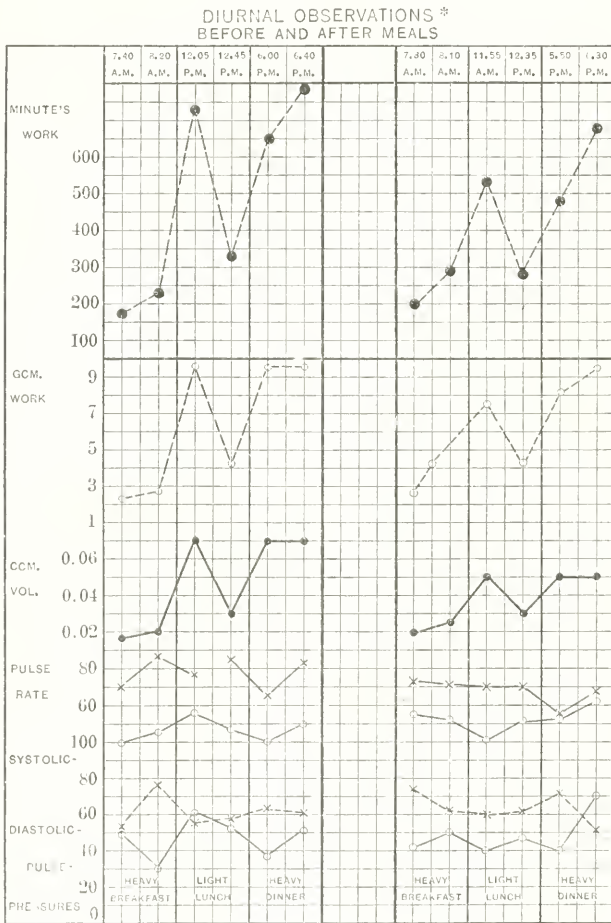
* ESTIMATIONS MADE WITH VOLUMBOLOMETER AT SANTA BARBARA, CAL.

CHART 6

"In the final result of the estimated pulse work all these cause negative errors which are responsible for the unsatisfactory results that you describe. In general it is evident that with a strong pulse

and high values of pulse work the loss of energy is more difficult to prevent than with low values.

"It seems to me that you can very well utilize your own clinical observations in so far as they concern comparative observation on the same patient, but I should much regret your publishing incorrect



* ESTIMATIONS MADE WITH VOLUMOLOMETER AT SANTA BARBARA, CAL.

CHART 7

results, the cause of which errors I have just explained. Such results would better be withheld. Confusion would only result and not only pressure bolometry, but all sphygmobolometry be freshly discredited. The general medical public is neither discriminating nor sufficiently oriented to draw correct, even if not entirely erro-

neous, conclusions. Hence, I do not believe such an inclusion would accomplish the purpose mentioned in your letter, of furthering the method. Sphygmobolometry merits support, and although it has

DIURNAL OBSERVATIONS*
BEFORE AND AFTER MEALS

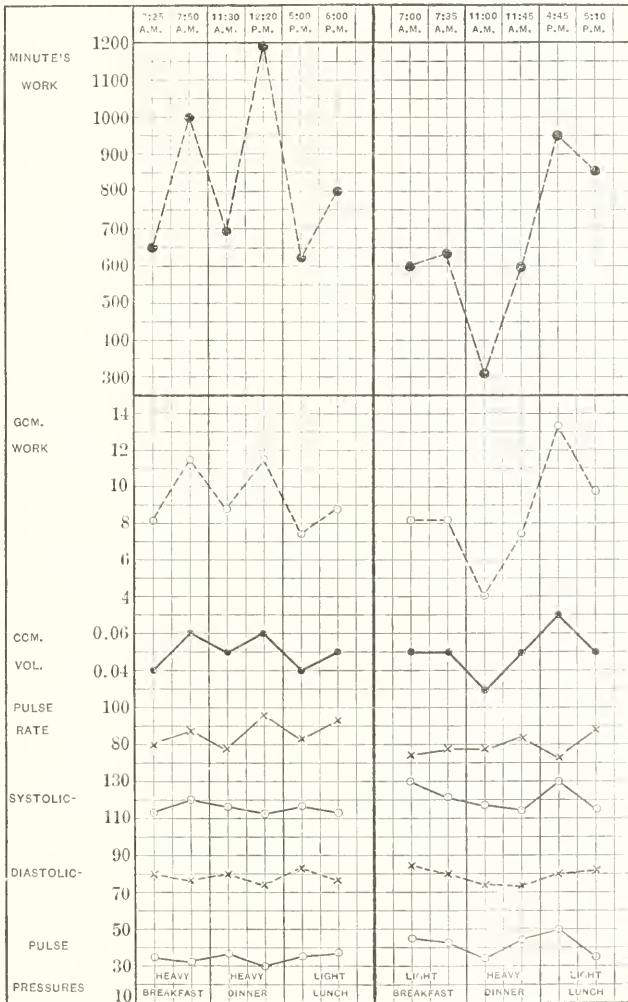


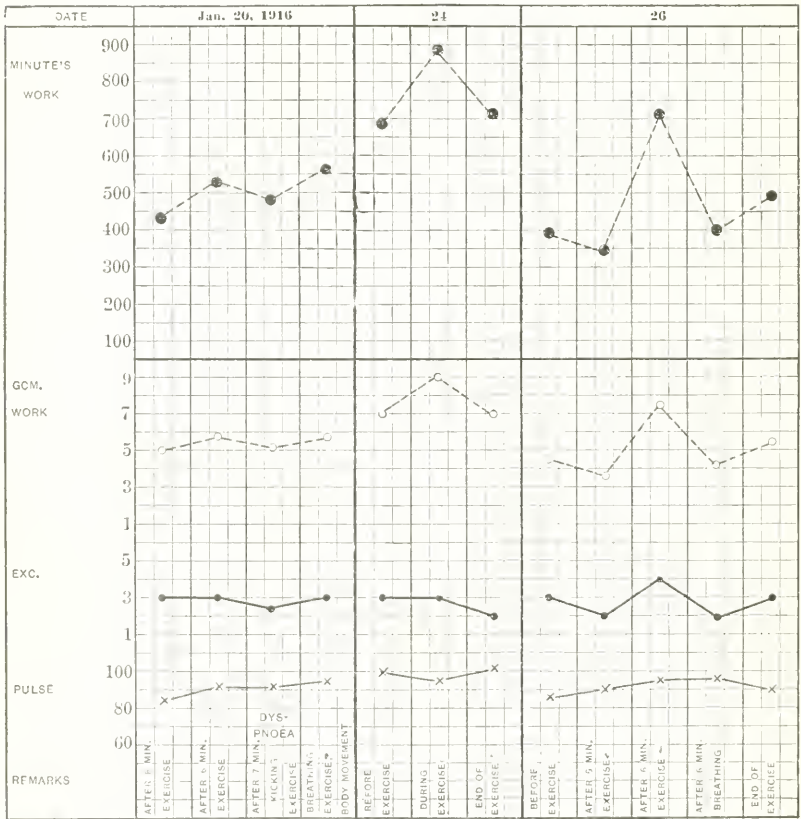
CHART 5

not yet attained an undisputed place in stricken Europe, it should acquire such recognition in unprejudiced America. For the moment most of the great medical public unintelligently regard the method

as entirely useless, but I am convinced that eventually sphygmology will entirely reform clinical hydraulics, although by then I shall probably have passed away."

One final caution, from the patient's standpoint, is worth mentioning. I have repeatedly observed, especially in high strung, sensitive patients, with high blood-pressure and broad excursions

INFLUENCE OF EXERCISE*

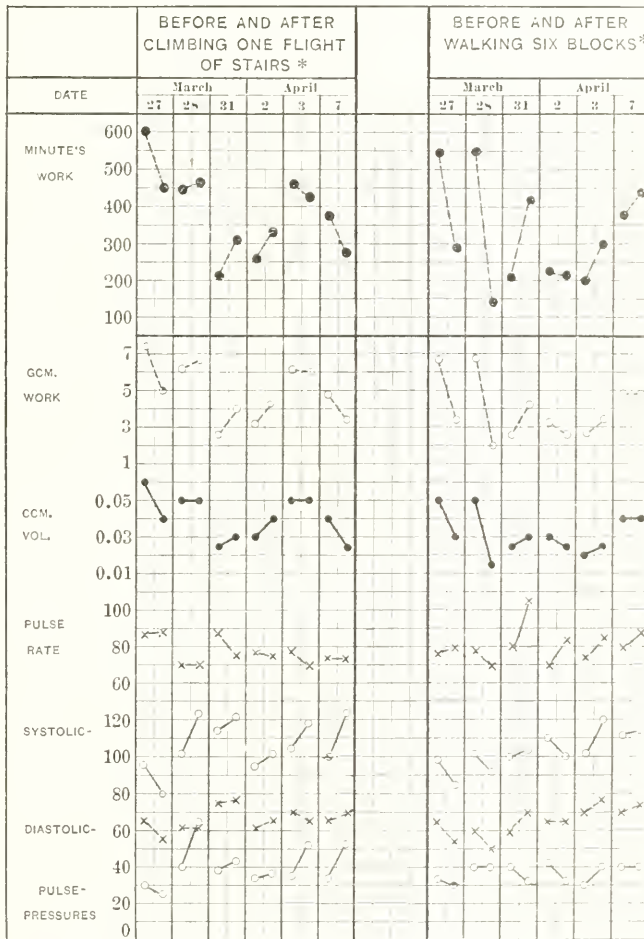


* ESTIMATIONS MADE IN NEW YORK

CHART 9

of the transmitted beat, so decided a trepidation, dread, or fear while watching this lively, extensive oscillation of their own pulses as to render any such series of determinations quite inadvisable from the point of view of their proper treatment. It seems to have quite the same effect as in the old days when similar patients builded their happiness or misery upon the presence or absence of albumin and casts in their urine.

PERMANENCY OF AN INDIVIDUAL'S PULSE WORK. Charts 4 and 5 tend to show that in the ordinary individual the figures for the Work or Volume do not vary to any striking degree, in the course of a brief number of years. Most of these observations were made



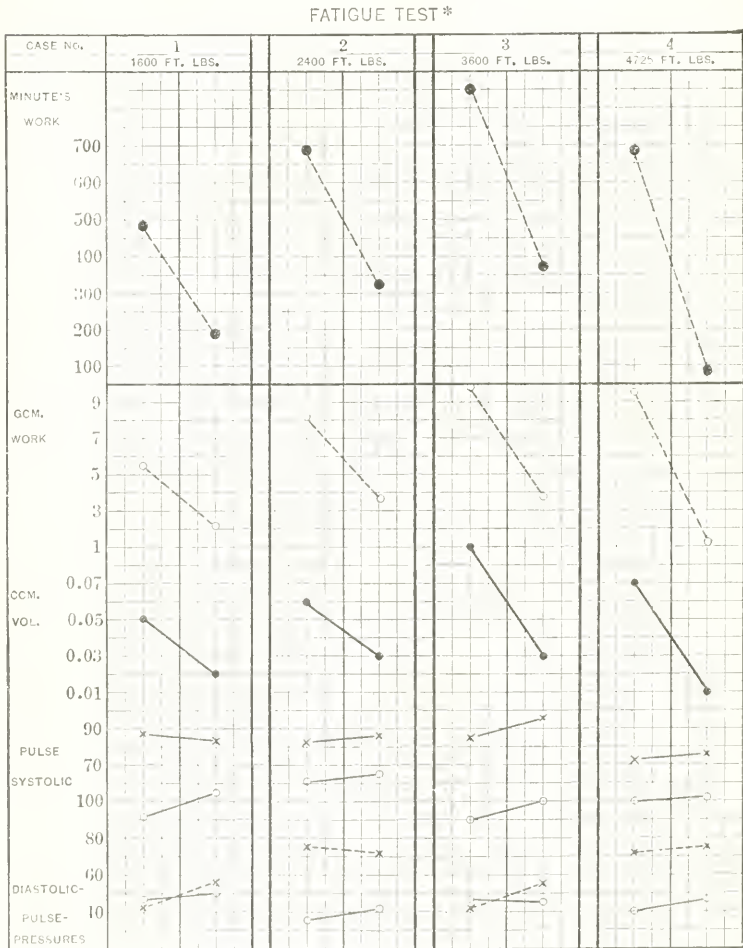
* ESTIMATIONS MADE WITH VOLUMBOLOMETER AT SANTA BARBARA CAL.

CHART 10

before and after various forms of exercise, and although the response to exercise may vary with variations in the patient's condition, the limits within which these variations occur remain fairly constant, in spite of the fact that observations were made both in New York

and in Santa Barbara, California, with entirely different instruments and several different observers.

VARIATIONS DEPENDENT UPON EXTRAMEDICINAL INFLUENCES. Pulse volume and heart work vary with the ordinary daily procedure and happenings of normal life, such as posture, activity, exercise,



* ESTIMATIONS MADE WITH VOLUMBOLOMETER AT SANTA BARBARA, CAL.

CHART 11

eating, drinking, bathing, nervous excitement, rest, fatigue, etc., so that to determine if one or both of these definitely measurable dynamic qualities of the pulse can be utilized in estimating circulatory efficiency, we have made a certain number of estimations upon

normal and diseased individuals before and after such influences. It ought to be helpful, for example, if a certain individual can run up so many stairs in a given time and show no effect of fatigue; and if an increase in the number of stairs, or the speed with which they are traversed results in a moderate increase in *minute work*, we would presumably consider the circulatory response as relatively efficient; but if, at the second flight of stairs, the *minute's work* which

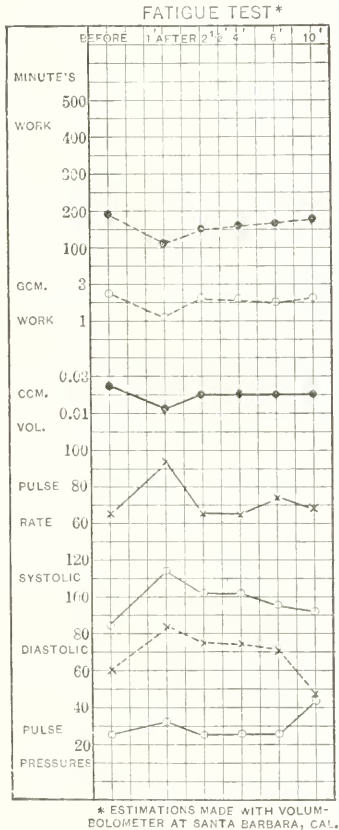


CHART 12

had been moderately increased after one flight, suddenly fell, and especially if at the same time the pulse-rate considerably increased, such a result would evidently mean fatigue, and point to a relatively inefficient circulation.

Chart 6 exhibits the difference in *minute's work*, in two normal individuals in the horizontal, sitting and vertical postures. In changing from a horizontal to a sitting posture there is typically a

considerable decrease in minute's work, which is usually brought about by a decrease in pulse volume. The minute's work increases again, however, when the subject assumes the vertical position.

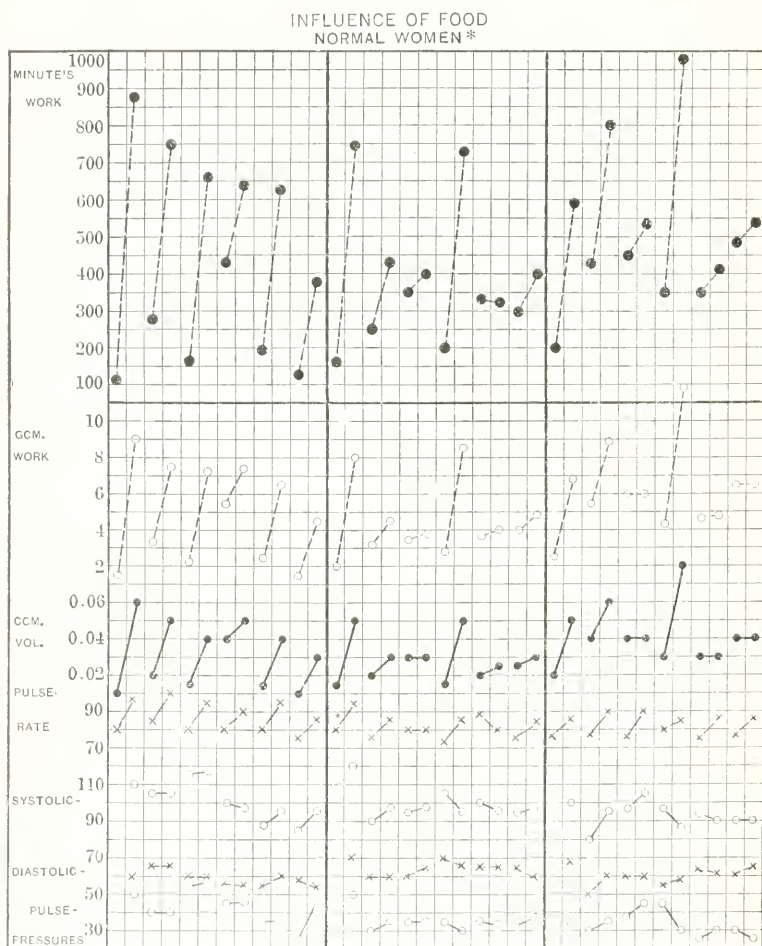


CHART 13

Charts 7 and 8 represent the difference in *minute's work* in four individuals in the early morning, before breakfast, after breakfast and before and after the midday and evening meals. The similarity of the curves in Chart 7 is quite striking. The lowest points of the curves of work, minute's work and volume are all at the early

morning reading. This is followed by a slight rise after the ingestion of food. The activities of the day and increase in temperature of a very relaxing summer day, result in markedly higher readings

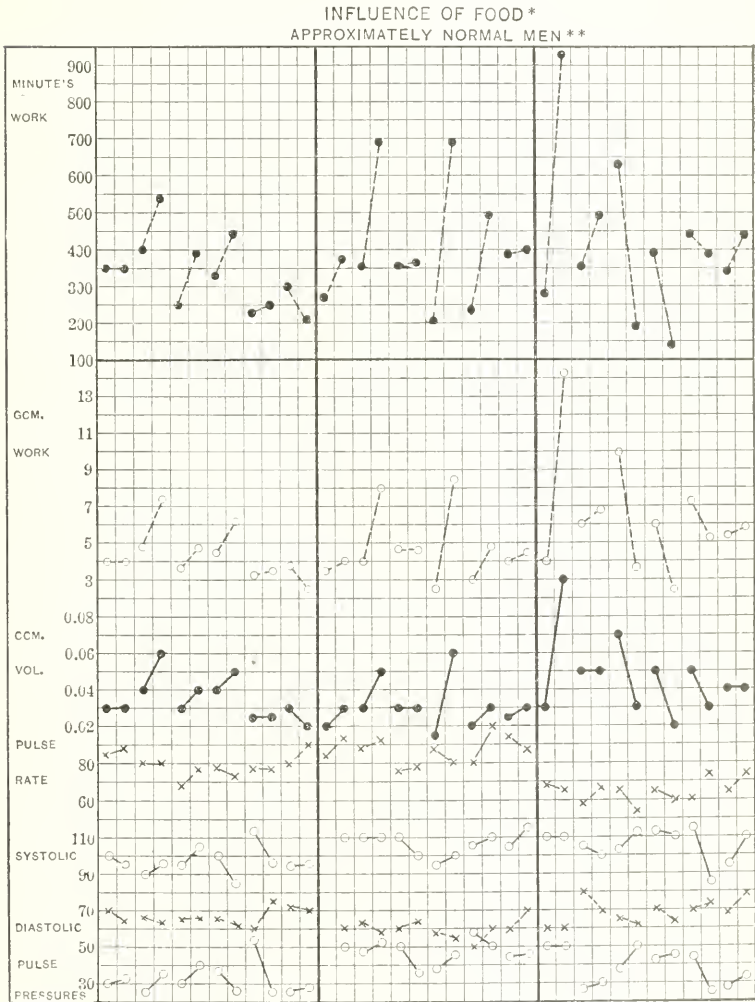


CHART 14

at noon, but these high readings are followed by a drop after the noon meal. In the evening again the readings are high, followed by a further increase in minute's work after the evening meal, this

increase being due to an increase in pulse-rate rather than to any change in volume. The observations illustrated by Chart 8 were made upon nurses, interrupted at their work, where influences other than food were probably present. There is, however, a general

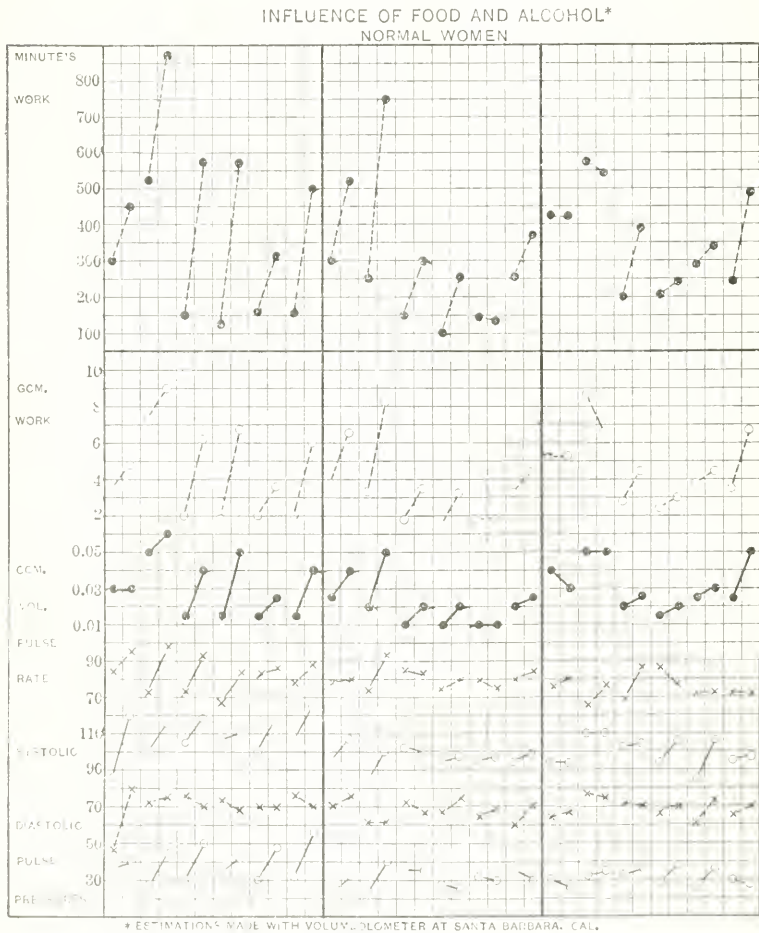


CHART 15

tendency for the minute's work to increase after meals. These observations were made on a cool, bracing day when there was little change in temperature during the day.

Charts 9 and 10 represent the effect of some different types of exercise in two normal individuals. Here the normal reaction to exercise is an increase in minute's work, generally accompanied by

a corresponding increase in gram centimeter's work and in volume. Where there is a decrease in minute's work it indicates fatigue.

Chart 11 shows the effect of fatigue on four normal subjects. The readings were taken before and as soon after exercise as it was

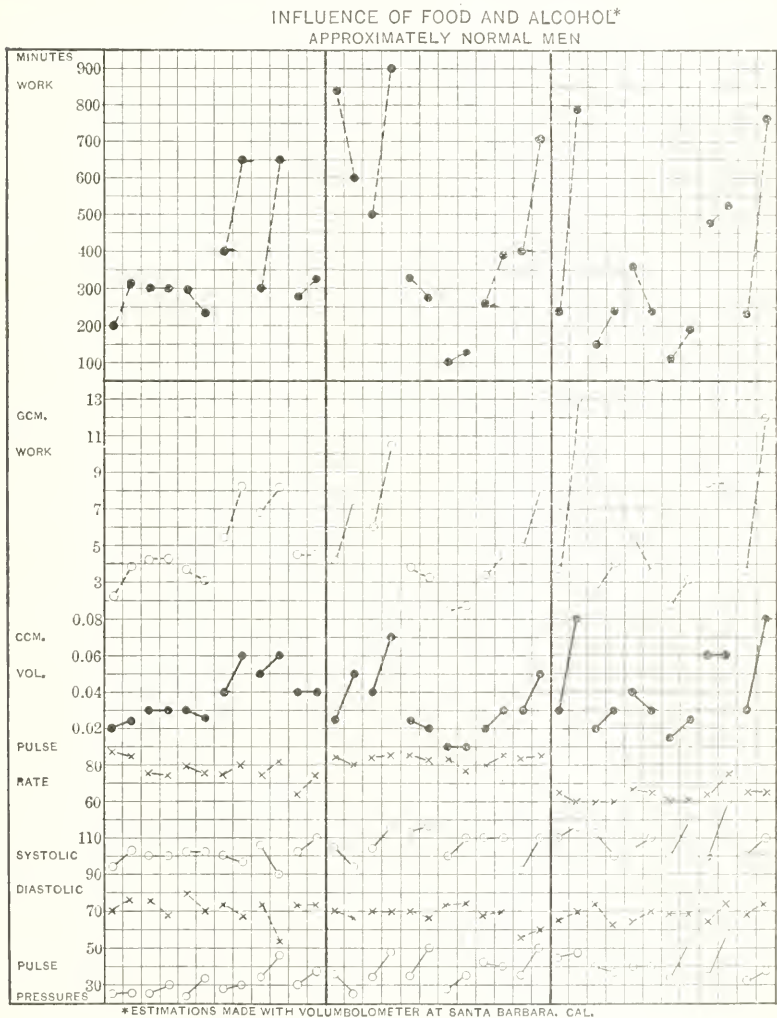


CHART 16

possible to adjust the cuff; thereby obtaining a marked decrease in work and minute's work.

Chart 12 shows the effect of fatigue and the gradual return to

normal after the initial decrease in work. Readings were taken at intervals of one minute, two and a half, four, six and ten minutes after exercise.

Charts 13 and 14 represent the effect of food in six individuals. There is generally a marked rise in minute's work, gram centimeter's work and volume after the ingestion of food; and this is especially well shown in Chart 13 where the subjects are more nearly normal than those of Chart 14.

Charts 15 and 16 represent the effect of food in these same individuals, under similar conditions, at the same time of day, when this food was supplemented by a certain amount of alcohol. There is less regularity in the results obtained in these two charts than in the two preceding, uncomplicated food charts, but the general or average tendency toward a rise after the meal is the same.

SUMMARY. 1. It is evident that the method of volume bolometry is relatively simple, easily applicable, not unduly time-consuming and of at least practical accuracy.

2. To determine whether the results obtained therefrom are sufficiently valuable either in estimating circulatory efficiency, *i. e.*, a functional circulatory test, or in following, or judging the effect of medicinal, or extra-medicinal methods of treatment, more clinical experience under a greater variety of conditions must necessarily be available.

3. It suggests a new conception of the circulation and certainly is worth further study.

4. It is better adapted to clinic or perhaps to office practice than to routine private practice at a patient's home.

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THE RAPIDITY AND PERSISTENCE OF THE ACTION OF DIGITALIS ON HEARTS SHOWING AURICULAR FIBRILLATION.¹

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THE fact that digitalis requires many hours or even days to affect the heart when given in the usual doses, has been perhaps the chief disadvantage in the use of the drug in cases of heart disease in which prompt action is urgently indicated. It is well known that repeated doses must be given before the action of the drug manifests itself, and it is often difficult to determine accurately when the action begins. There has also been considerable discussion as to how long the drug remains effective after its administration is stopped, a point of important bearing on the so-called cumulative action of the drug.

In order to gain further knowledge regarding these questions, the effect of large single doses of digitalis has been observed on a selected group of patients suffering from a form of cardiac disorder which is definitely influenced by the drug. All the cases studied were demonstrated by electrocardiograms to suffer from either auricular fibrillation or auricular flutter, and in all the ventricular rate was abnormally rapid. Care was taken in every case to make sure that the patient was not under the influence of digitalis when the large dose was administered, either by the history, or the statement of the physician sending the patient into the hospital, or by a period in the hospital of at least ten days without the administration of the drug.

Digitalis was given by mouth in the form of the tincture and the dose was regulated according to the method worked out by Eggleston.² The underlying principle of this method is to give in one or several frequent doses the entire amount of the drug which may be expected to produce the maximum therapeutic effect. The tincture of digitalis used was purchased from a reliable manufacturer and

¹ Read before the Association of American Physicians, Atlantic City, June 17, 1919.

² Digitalis Dosage, *Arch. Int. Med.*, 1915, xvi, 1.

each lot of the drug was standardized by the "cat method," described by Hatcher and Brodie.³

It was found that 1 c.c. of the tincture injected intravenously was approximately the lethal dose for one kilo of body weight of the cats used, and following Eggleston's results, 0.15 c.c. was given for each pound of body weight of the patients. The dose, amounting to 15 c.c. per hundred pounds, was the maximum, and was usually given as a single dose, although in some of the earlier cases

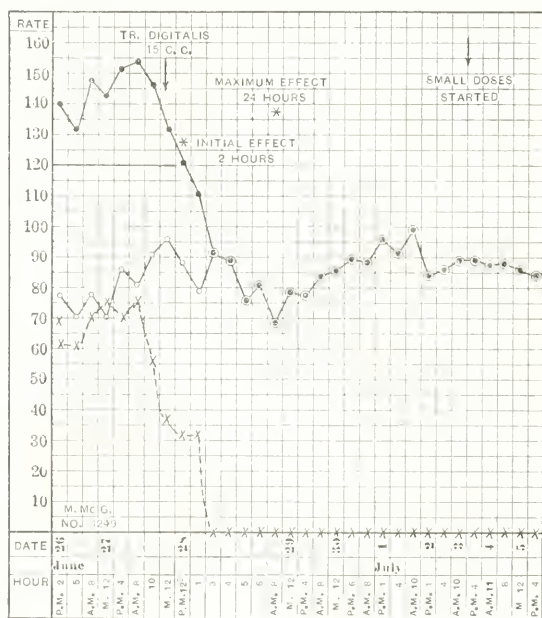


CHART I.—Case 9 of Table. Mitral stenosis and auricular fibrillation. The upper solid line indicates the heart-rate counted by means of the stethoscope placed over the apex-beat. The lower solid line indicates the radial pulse-rate. The broken line indicates the pulse deficit or the number of cardiac contractions that could be heard per minute, which produced no palpable pulsation in the radial artery. The time when the single dose of digitalis caused the initial and maximum effects are indicated. The increase in the rate of the radial pulse and the fall in the pulse deficit with the decrease in the heart-rate are well shown. Initial effect in two hours. Maximum effect in twenty-four hours. Duration of effect not determined.

the dose was divided into three or more parts and given four to six hours apart. The clinical results obtained in giving large single doses of the drug to about 100 patients have been convincing of the correctness of Eggleston's work. This will be demonstrated also by the cases tabulated in this paper. The doses usually ranged from 15 c.c. to 25 c.c. of the tincture.

The patients forming the basis of this paper were studied during continuous rest in bed. The heart rate was counted several times

³ Biological Standardization of Drugs, Am. Jour. Pharm., 1910, lxxxii, 360.

a day by a member of the medical staff, using the stethoscope over the heart, for a number of days whenever the withholding of the drug seemed justified. The radial pulse was also counted, and these findings, together with the pulse deficit (the difference between the heart and radial rates), were charted. After the digitalis was given similar counts were frequently made, in some cases at fifteen-minute intervals, for several hours. The results of three observations are shown in the accompanying charts.

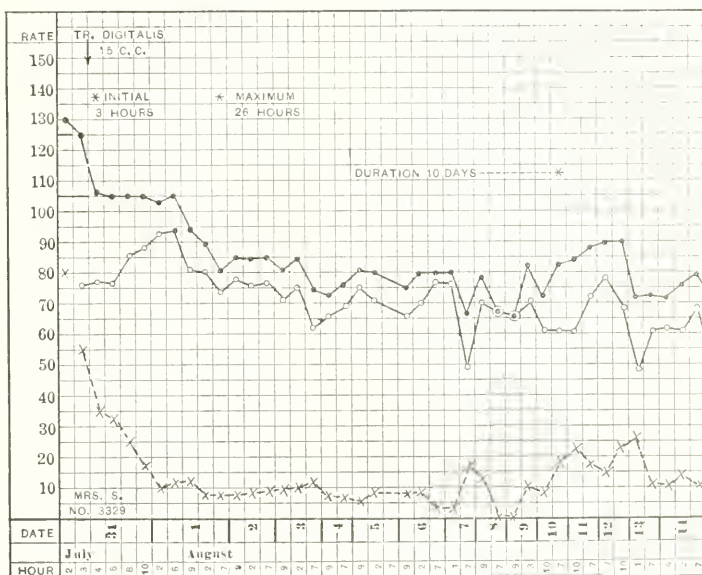


CHART II.—Case 11 of Table. Mitral stenosis and insufficiency, chronic myocarditis and auricular fibrillation. The three lines have the same significance as those in Chart I. The time when digitalis began to be ineffectual is indicated by the increase in the heart-rate which began ten days after the administration of digitalis. Initial effect in three hours. Maximum effect in twenty-six hours. Duration of effect ten days.

The well-known effect of digitalis in slowing the ventricular rate in cases of auricular fibrillation was used as indicating the action of the drug, and practically all of the cases included in this paper showed an abnormally high ventricular rate before digitalis was given. Two cases of auricular flutter are exceptions to the foregoing procedure, and here the disappearance of flutter, as demonstrated by electrocardiograms, was taken as evidence of digitalis action.

Twenty-six cases were studied and tabulated.

In 16 cases the observations were made at intervals sufficiently frequent after the single dose of the drug was given to determine accurately the time when the digitalis became effectual. The drug was considered to have affected the heart when the ventricular rate first became slower than it had been at any time previous to

the administration of digitalis and when the ventricular slowing continued, so that the rate of the ventricles assumed a definitely new level. In 2 cases the permanent disappearance of auricular flutter was taken as the indication that the drug had affected the heart. In all of the 16 cases so observed the heart was affected by digitalis in from two to five hours after the oral administration of a single large dose of the tincture.

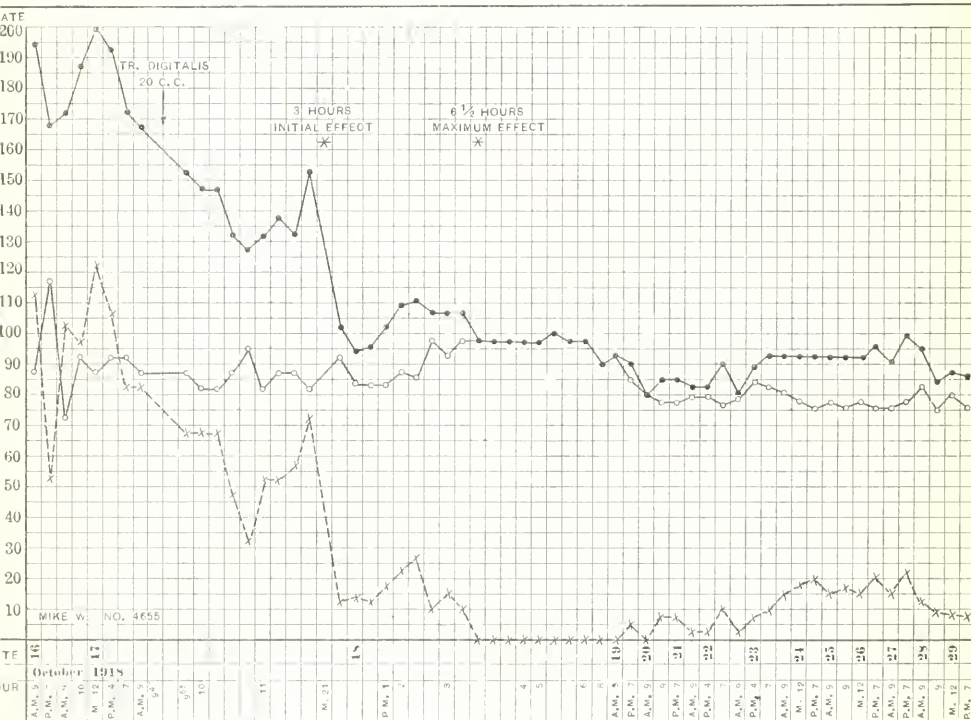


CHART III.—Case 25 of Table. Syphilis, chronic myocarditis and aortitis. The three lines have the same significance as in Chart I. Single dose of 20 c.c. of the tincture given. Initial effect in three hours. Maximum effect in six and a half hours. Heart-rate remained slow for twenty-two days.

The maximum effect of digitalis was considered to have occurred when the ventricles attained approximately their slowest rate and when the pulse deficit had disappeared or reached its lowest count. It was usually quite clear when the maximum effect occurred, but in some cases in which frequent heart-rate counts were not carried on long enough the maximum effect can only be approximated. The charts from the 26 cases studied indicate there is some difference in the length of time required for a single large dose of digitalis to produce the maximum effect on cases of auricular fibrillation, and the cases fall into two groups.

No.	Sex.	Age.	Wt.	Diagnosis.	Dose.	Before.	Heart-rate.		Duration.
							Onset time.	Maximum effect.	
1	M.	62	124	Arterial sclerosis; mitral insufficiency; chronic nephritis	17 c.c.	85	?	60, 24 hr.	7 days.
2	F.	52	127	Arterial sclerosis; mitral insufficiency; chronic nephritis	18.5 c.c. in 4 doses	120	?	80, 20 hr.	8 days small doses started
3	M.	48	172	Mitral stenosis and insufficiency	22 c.c. in 3 doses	160	106, 13 hrs.	80, 23 hr.	10 days.
4	F.	49	151	Mitral stenosis and insufficiency; chronic nephritis	22 c.c. in 3 doses	142	165, 5 hrs.	92, 24 hrs.	6 days small doses started.
5	M.	57	190	Mitral insufficiency; myocarditis; chronic nephritis	29 c.c. in 3 doses	135	?	76, 15 hrs.	3 days small doses started.
6	M.	72	137	Arterial sclerosis; chronic nephritis	15 c.c. in 3 doses	130	?	90, 24 hrs.	8 days small doses started
7	F.	45	140	Myocarditis; chronic alternans; auricular flutter	20 c.c.	148	102, 3½ hrs.; flutter changed to fibrillation	90, 24 hrs.	13 days.
8	M.	63	110	Arterial sclerosis; chronic nephritis	6 c.c.	132	80, 3 hrs.	80, 3 hrs.	5 days small doses started.
9	F.	35	106	Mitral stenosis	15 c.c.	145	120, 2 hrs.	68, 24 hrs.	5 days small doses started.
10	M.	57	138	Arterial sclerosis; myocarditis; chronic nephritis	9.5 c.c. 5 days after 19 c.c.	Flutter replaced by normal rhythm in 3½ hrs.			after 9 days in hospital.
11	F.	36	100	Mitral stenosis and insufficiency; myocarditis	15 c.c.	130-140	105, 3 hrs.	80, 26 hrs.	11 days.
12	F.	47	110	Mitral stenosis and insufficiency; cystic goitre	15 c.c.	130-160	110, 3 hrs.	85, 22 hrs.	8 days.
13	M.	54	156	Arterial sclerosis; myocarditis	10 c.c., 5 c.c., 3 days later	120	?	82, 18 hrs.	13 days after 2d dose
14	M.	37	135	Mitral stenosis and myocarditis	20 c.c.	120-150	?	84, 20 hrs.	5 days, 2d dose given.
15	F.	49	130	Exophthalmic goitre; myocarditis	20 c.c.	110-125	?	95, 24 hrs.	6 days.
16	F.	43	178	Mitral insufficiency	18 c.c.	112-160	90, 5 hrs.	80, 8 hrs.	2 days mechanism became normal.
17	M.	49	139	Arterial sclerosis; myocarditis; mitral insufficiency	20 c.c.	120	108, 3 hrs.	87, 14½ hrs.	9 days, 2d dose given.
18	F.	42	122	Mitral stenosis and insufficiency	15 c.c.	75-135	60, 3 hrs.	38, 24 hrs.	15 days.
19	F.	60	74	Mitral stenosis and insufficiency	6 c.c.	150-165	114, 2 hrs.	100, 2½ hrs.	4 days death.
20	F.	23	132	Mitral stenosis and insufficiency; aortic stenosis	6 c.c.	95-115	80, 2 hrs.	55, 6 hrs.	10 days patient discharged
21	M.	62	121	Myocarditis and chronic nephritis	15 c.c.	120-128	?	91, 8 hrs.	9 days patient discharged
22	F.	54	198	Arterial sclerosis; myocarditis; chronic nephritis	10 c.c. 2d dose 10 c.c.	175-180 150-175	160, 1½ hrs. 105, 5 hrs.	120, 22½ hrs.	30 hrs., 28 hrs.
23	M.	42	168	Myocarditis; syphilis	20 c.c.	120-150	118, 3 hrs.	70, 24 hrs.	4 days.
24	M.	40	120	Mitral stenosis and insufficiency	20 c.c.	135-160	102, 3 hrs.	112, 7 hrs.	6 days.
25	M.	48	165	Myocarditis; syphilis; aortitis	20 c.c.	167-207	110, 24 hrs.	96, 6½ hrs.	22 days patient discharged
26	F.	37	?	Mitral stenosis and insufficiency; myocarditis	15 c.c.	130-140	110, 24 hrs.	70, 9 hrs.	4 days patient discharged.

In the first group of 19 cases the maximum effect of the drug occurred in from fifteen to twenty-six hours. In a second smaller group of 6 cases the maximum effect occurred in from six to nine hours. The cause of the difference between the two groups is not apparent. In a case of auricular flutter in which the normal cardiac rhythm supervened after digitalis was given no statement as to the maximum effect can be made.

In order to determine the length of time which the drug controlled the heart the patients were kept constantly in bed and the ventricular rates were counted by the stethoscope several times a day. When the ventricular rate began to accelerate and the pulse deficit to increase the drug was considered to have begun to be ineffectual. At this time another dose of digitalis, usually half the amount originally given, was followed by a prompt fall in the ventricular rate and in the pulse deficit. The rise in the ventricular rate was practically always accompanied by an increase in the symptoms of cardiac inefficiency.

In 12 cases in which the time when the drug began to be ineffectual was clearly indicated, digitalis affected the heart for from four to fifteen days, the effect lasting on an average of nine days and six hours. In 1 case the ventricular rate remained slowed for twenty-two days, when the patient was discharged from the hospital without receiving another dose of the drug, although the primary effect had been very striking. In another case the ventricular rate began to accelerate thirty and twenty-eight hours respectively after each dose of 10 c.c. of the tincture, given several days apart. In the remaining 12 cases no statement regarding the duration of the effect can be made, as subsequent doses of the drug were given before the effect of the initial dose had begun to diminish, or, as in 1 case in this series, the patient died four days after the initial dose.

From this series of cases it may be stated, however, that although the effect of a single large dose of the tincture of digitalis on the heart is not constant, it usually lasts from four to fifteen days, and averages nearly ten days.

The persistence of the action of digitalis is of considerable practical importance, and has been the subject of several investigations. Hatcher⁴ has shown that various digitalins vary in their persistence in experimental animals and that the persistence also varies markedly in different animals. He showed that the effects of digitonin and digitalis persist longer than do those of the other digitalins in common use, especially in cats. He found that the effects of a single large dose of these drugs, administered intravenously, may persist for a full month. Cohn, Fraser and Jamison⁵ investigated this subject, determining the persistence of the drug administered orally

⁴ The Persistence of Action of the Digitalins, *Arch. Int. Med.*, 1912, x, 268.

⁵ The Influence of Digitalis on the T-wave of the Human Electrocardiogram, *Jour. Exp. Med.*, 1915, xxi, 593.

to patients by the change in the T-wave of the electrocardiogram. They found that this change, which was brought about by digitalis, persisted for from five to twenty-two days after the administration of the drug was stopped. Although this method of determining the effect of digitalis was not consistently followed in our series of cases, the impression was gained from several cases so studied that the return of the T-wave of the electrocardiogram to the form present before digitalis was given occurred a day or two later than the acceleration of the ventricular rate.

Eggleston⁶ has also been among those who have studied the duration of digitalis action in man. He determined the length of time that various cardiac disturbances produced by the drug persisted and found that coupled beats (regularly recurring premature ventricular contractions) persisted for from four to twelve days after digitalis was discontinued, while other disturbances of the cardiac mechanism caused by digitalis persisted for a shorter length of time.

A matter that has been frequently discussed regarding the effect of digitalis when administered by mouth has been the question of the rapidity of its absorption from the alimentary tract. The study of our series of cases seems to throw some light upon this subject. It has been customary to consider the absorption of digitalis from the alimentary canal as irregular, slow and uncertain and the factor of absorption has been called upon to explain differences in the amounts of the drug required to produce the same effects in different individuals. Recently, Wedd⁷ found there was a wide difference in the amounts of digitalis necessary to produce certain toxic effects in different individuals, the individual variation being from 20 c.c. to 100 c.c. of the tincture given in large but not single doses. The variation, he believes, is due to variations in absorption. There is, no doubt, definite difference in the rapidity of absorption of different digitalis preparations, as Haskell, McCants and Gardner⁸ have shown experimentally, and they find that the tincture is better absorbed from the gastro-intestinal tract than the infusion, and is equally as well absorbed as other preparations.

Eggleston concluded from his study of the effects of large doses of the drugs that digitonin was more completely absorbed than digitalis, but, nevertheless, he found that both of these preparations are probably rapidly and fairly uniformly absorbed from the alimentary canal of man.

The fact that a single large dose of the tincture of digitalis uniformly affected the heart of all of the cases in our series in which its

⁶ Clinical Observations on the Duration of Digitalis Action, *Jour. Am. Med. Assn.*, 1912, lix, 1352.

⁷ Observations on the Clinical Pharmacology of Digitalis, *Bull. Johns Hopkins Hosp.*, 1919, xxx, 131.

⁸ The Rate of Absorption of Various Digitalis Preparations from the Gastro-intestinal Tract, *Arch. Int. Med.*, 1916, xviii, 235.

initial effect could be determined in from two to five hours, offers a strong argument for the fairly rapid and uniform rate of absorption from the alimentary tract of patients with heart disease. It is true that the maximum effect did not show so uniform a relation to the time of administration, but it seems probable that factors other than absorption may have been responsible for the variations in the time required for the maximum effect to occur.

It is this rapid and uniform rate of action of the drug when administered in large single doses as herein described, which especially commends the use of digitalis in this manner therapeutically. It is felt that further studies are required before such large doses as were given should be recommended for general use, especially when patients are not under constant observation in hospitals. But the method has been sufficiently tried so that it seems entirely justified whenever rapid digitalis action is strongly indicated, and our experience leads us to believe that it is a much safer method of obtaining rapid digitalis action than the intravenous administration of digitalis bodies, especially strophanthin. Nearly all the cases reported in this series showed very striking clinical improvement within a few hours after the administration of the single large doses of the tincture of digitalis. It is particularly on this account that it is felt that Eggleston's conclusions as to the dosage of the drug are essentially correct.

SUMMARY. A series of 26 cases of auricular fibrillation or flutter are reported, to which large single doses of the tincture of digitalis were administered by mouth. The drug used was standardized and was usually given in doses ranging from 15 c.c. to 25 c.c.

The study of these cases demonstrates that such doses of digitalis affect the heart of cases of auricular fibrillation or flutter at a relatively constant time after administration, in from two to five hours, indicating that the drug is absorbed from the alimentary tract at a fairly rapid and uniform rate. The series of cases also demonstrates that the maximum effect on the heart is usually obtained in about twenty-four hours and generally continues to be effectual for from four to fifteen days, or on an average of nearly ten days.

REVIEWS.

EXPERIMENTAL PHARMACOLOGY. By HUGH MCGUIGAN, PH.D., M.D., Professor of Pharmacology in the University of Illinois, College of Medicine, Chicago. Pp. 250; 56 engravings; 7 colored plates. Philadelphia: Lea & Febiger, 1919.

THIS is, to quote the author, "an attempt to present experimental pharmacology in a brief, concise form, yet give the student an adequate view of the field." The book contains a summary of the main facts of pharmacology, in outline form, with directions for illustrative experiments, arranged with regard to the action of drugs on the various physiological systems. The introductory chapters contain general information to be found in standard text-books, and will be valuable to supplement a course of didactic instruction. The outlines of major facts of pharmacology suggest the "quiz compend" method and are not conspicuously good. Accompanying these outlines are directions for some 320 illustrative experiments, the performance of all of which, while of undoubtedly great value, would be quite beyond the time available in the usual course of instruction. The author, however, suggests elimination or division, but does not indicate clearly just how this can be accomplished so as to return the greatest possible benefit to the student. The arrangement is at times unusual: the anesthetic action of ether and chloroform and the action of the alcohol-chloral group on reflexes are discussed with digitalis and the nitrites under Pharmacology of the Heart and Blood-pressure; experiments with bromides and cannabis are given in the chapter on the closed method of anesthesia; epinephrin is listed in the chapter entitled antagonism. Few experiments of an analytical character are included, most of them being aimed rather at an exposition of the action of the drug than an analysis of the precise method in which these effects are produced. The chief fascination of pharmacology, as a field of investigation, lies in experiments of the latter type, and it is unfortunate that the student entering this field for the first time should be left unaware of its legitimate pleasures. Nevertheless, these criticisms aside, the book is decidedly a departure in the right direction. It emphasizes to the student the value of experimental pharmacology and furnishes a much needed scientific background for the study of applied therapeutics.

C. F. S.

PHYSICAL DIAGNOSIS. By RICHARD C. CABOT, Professor of Medicine, Harvard University. Seventh edition. Pp. 527; 263 figures and 6 plates. New York: William Wood & Co., 1919.

THIS book does not need an introduction, as it has long been recognized as one of the foremost books upon physical diagnosis. It is founded upon good, sane clinical judgment with two underlying basic principles, thoroughness and common-sense. Dr. Cabot puts forth the basic principles of physical diagnosis, and in no case does he claim overexaggerated evidences from any one physical finding.

In this volume much new material has been added. Cardiac signs of nervousness as exemplified by the D. A. H. cases are given the proper interpretations. It is pointed out that the simple goitre will sooner or later cause cardiovascular changes similar to those due to syphilis or other causes. This is always associated with an elevation of the systolic pressure with myocardial changes and of very slow development (average fourteen years). The diastolic pressure in these cases remains little if at all elevated. In the toxic goitre these changes are more rapid and usually come on within a year. Dr. Cabot again puts forth the growing idea that in the rheumatic endocarditis cases there is always an association or combination of stenosis and regurgitation. He also goes further and believes that practically all these cases are due to some variety of the streptococcus. Hilus tuberculosis is brought into a place of importance but again the word of caution is given that unless there is an association of symptoms the diagnosis should not be made as to its being active. It is pointed out that these are childhood infections, starting in the deep tissues around the hilus and there remaining dormant until adult life is reached. This is undoubtedly one of the most important factors set forth in the book, as these comprise a large number of the so-called "closed cases of tuberculosis" discovered in the course of a roentgen-ray examination.

It is to be regretted there are so many typographical errors in this most important book, but, nevertheless, this does not detract from the vast amount of most important knowledge contained therein.
T. K.

THE FUTURE OF MEDICINE. By SIR JAMES MACKENZIE, Consulting Physician to the London Hospital. Pp. 238. London: Oxford University Press, Henry Frowde and Hodder & Stoughton, 1919.

THIS little volume comes at the close of the active career of one of the foremost clinicians and investigators in clinical medicine now living. He has detailed the circumstances that led him to undertake his researches and the methods employed in carrying them out.

He has found much to criticise in medical education, research and clinical medicine as conducted at present.

The principal point of attack has been on the so-called ideal of medicine, dominant today, which is alleged to depend upon the revelation of the signs of disease by some mechanical contrivance devised in the laboratory. This trend in modern medicine has been vigorously protested against on the ground that not only is the knowledge to be gained by laboratory methods liable to be misleading if not carried on in conjunction with careful clinical observation, but that what value it has is limited to the late stages of disease after structural signs have developed. Real progress depends upon the detection and study of disease in earlier stages. Our medical education and research should therefore be adjusted to this viewpoint, and the study of symptoms, which are at present little understood, should assume the position of great importance it deserves. The general practitioner is said to have the best opportunity for research, and he should be educated to take advantage of his opportunity. In the hospital the out-patient department should receive the attention of the trained physician, for here he can study the beginnings of disease; in the ward he finds the end-results.

No one interested in medicine will fail to find much of value in this book. Many statements will encounter more or less general dissent, such as the claim that laboratory training unfits men for work as physicians. Nevertheless, the position and attainments of the author have enabled him to point out, as perhaps no other could have done, the dangers of subservience to laboratory methods; the fallacy of attempting to draw deductions of clinical application from data obtained solely by mechanical contrivances; the importance of directing our energy to studying the beginnings of disease and the value of methods, which in his hands, have led to such important contributions to medical knowledge.

C. C. W.

THE WHOLE TRUTH ABOUT ALCOHOL. By GEORGE ELLIOT FLINT.
Pp. 294. New York: Macmillan Company, 1919.

HERE are set forth the views and experiences of one who is greatly impressed with the virtues of alcohol. To quote his own words: "Alcohol does not ruin men, men disgrace alcohol. Alcohol does not produce deficiency; but original deficiency seizes upon alcohol and abuses instead of uses it, thereby perhaps increasing the original deficiency." Throughout the book, as the author discusses the various phases of the subject, he repeatedly returns to this idea, and for him this constitutes the whole truth.

W. H. F. A.

HINDU ACHIEVEMENTS IN EXACT SCIENCE. By BENOY K. SARKAR, Professor, National Council of Education, Bengal. Pp. 82. New York and London: Longmans, Green & Co.

THE great debt which the medicine of Western Europe owes to Arabian culture is generally acknowledged. Not so well appreciated is the fact that in many scientific matters the Hindus anticipated the Saracens, and in fact taught them. By the aid of human dissection, acquaintance with many drugs and a definite system of medical instruction the Hindus had made considerable advance in the natural history and treatment of disease while Europe was still sunk in superstition and barbarism. This book is a brief account of the scientific achievements of this old civilization and is of historical interest.

W. H. F. A.

PSYCHOSES OF THE WAR. By H. C. MARR, M.D., Lieut.-Col., R.A.M.C.; Fellow of the Royal Faculty of Physicians and Surgeons, Glasgow. Pp. 272; 60 illustrations. London, England: Oxford University Press, 1919.

THE author emphasizes the fact that no new types of mental disorders were brought to light in the recent war and no new technique of treatment evolved. However, in his study of over 18,000 cases of mental affections divided among officers and enlisted men of the British Army observed during the entire period of the war, he obtained much information upon mental conditions which, although recognized prior to the conflict, had been insufficiently investigated because of scarcity of cases. As a consequence the author has evolved a classification of mental affections which differs somewhat from those of our present accepted authorities.

Colonel Marr has apparently given great care to the construction of the book, which shows evidence of not having been very hastily written, as so many of the recent war books do. He cites many typical case histories as illustrative of the various types of mental and nervous disorders discussed. These add greatly to the clinical interest and aid in making the author's rather unique classification of mental affections more acceptable to the reader.

The book is in seven chapters, the first being an introduction dealing with the subject as a whole, the article on malingering and its detection being of particular interest. The second deals with the psychopathies, or the hereditary and constitutional psychoses. The third is devoted to a study of psychasthenia. The fourth and fifth, respectively, to mental deficiency (infantile) and mental enfeeblement (adolescent). The toxic psychoses (the confusional insanities) are discussed in the sixth and the organic psychoses ("the cerebropathies") in the seventh. A short appendix, dealing

with the nature and method of examination of the cerebrospinal fluid, is of interest to the student, as is also a very complete and ingenious diagram for mental case taking, which is appended after the index.

As a whole, the book will be of value to those who will have the opportunity of observing the many recurrent cases that will appear in civil practice following the closing of the army mental hospitals. It is also of value as a history of the types of mental affections which were dealt with in the great war.

F. H. L.

THE ANATOMY OF THE PERIPHERAL NERVES. BY A. MELVILLE PATERSON, M.D., F.R.C.S., Professor of Anatomy in the University of Liverpool. Pp. 165; 64 illustrations. London: Oxford Press, 1919.

THIS presentation of the subject of peripheral nerves was conceived by the late Professor Paterson while occupying the position of Assistant Inspector of Special Military Surgical Hospitals during the war. The object was to provide a brief account of the peripheral nerves, especially for those engaged in military orthopedic work. To this end are introduced schemata giving the position of origin of the branches of the nerves to the limb muscles. These are in the form of full-page line illustrations and achieve their purpose very well, although, as the author points out, they must be used with due caution. Useful diagrams are shown of the innervation of the skin and of the muscles of the limbs. In each of these, alongside the illustrations is given the name of the nerve and also the spinal segments from which its fibers are derived. This linking up the name of the nerve with its spinal origin is carried out consistently through the book. In addition to the subject of spinal nerves, which takes up the major part of the book (87 pages), a short consideration is given of the sympathetic system (20 pages) and of the cranial nerves (50 pages).

W. H. F. A.

A LABORATORY MANUAL FOR ELEMENTARY ZOOLOGY. BY I. H. HYMAN, Department of Zoology, University of Chicago. Pp. 140. University of Chicago Press, Chicago, 1919.

AN important feature of the premedical education in college is the study of zoology with laboratory exercises. The course with which premedical students usually begin is that of so-called elementary zoology. This introduces them to the actual seeing and manipulation of various forms of animals, and usually requires also the use

of the microscope. To guide and direct the hands and eyes of these beginners and to forestall some of the oft-repeated questions is the purpose of the present manual. That it will achieve its purpose seems without doubt, for there is a terseness and directness of expression that is unequivocal, and each direction is given in logical sequence. While primarily for the use of students at the University of Chicago, it could be utilized readily elsewhere. W. H. F. A.

THE MEDICAL AND SURGICAL ASPECTS OF AVIATION. By H. GRAEME ANDERSON, M.B., C.H.B., F.R.C.S., Surgeon, Royal Air Force, Central Hospital; Senior Assistant Surgeon, St. Mark's Hospital; Senior Assistant Surgeon, Belgrave Hospital. Pp. 255; 47 illustrations. London: Oxford Medical Publications, 1919.

THE first book to make its appearance after the World War is on a subject which received the most intense study during hostilities by groups of experts in all countries. Surgeon Anderson was what we called in our service a "Flight Surgeon," and in his book he has given us the results of his work with the flyers, the actual application of the various tests which were devised to prevent, as far as possible, airplane accidents and the onset of *aëroneurosis*. His observations throughout the book are very practical and his recommendations for prevention and treatment of each type of case arising in the flying service are well considered.

He deals with the selection of the flyer *per se* and with the management of the pilot after entering the service, from his training days to actual war-flying and his care and management after he has become "stale" or injured.

Collaborating with him, with chapters on applied physiology of aviation and the *aëroneuroses*, are Martin Flack, M.A., M.B., and Oliver H. Gotch, M.B., Ch.B., M.R.C.P., physician, Royal Air Force, respectively. Martin Flack (Physiology, Cambridge) was the foremost investigator in the new field of aviation medicine in England. His tests were adopted as standards and his tireless energy and enthusiasm had much to do with the success in selecting the wonderful personnel of the Royal Air Force.

In the future development of commercial aviation the problems of the flyer will more and more become of interest to the medical profession, and in this book the future "flight surgeons" will find a great many helpful suggestions. Starting with a historical review of medical interest in aviation, and giving the English standards for selection of candidates for the air service, together with the special chapters on applied physiology by Flack and the *aëroneurosis* by Gotch, Anderson then gives his experiences in *aëroplane* accidents,

beautifully illustrated by actual plates, including a photograph of the most remarkable accident which has occurred in which a sea-plane collided with and stuck in the mast of a large wireless station. A chapter on the surgery of aviation, in which he fully reports, with roentgen-ray plates, thirteen cases of "aviator's astragalus," is important.

Chapters on injuries and destructive effects of aeroplane bombs, on aeroplane dope-poisoning (tetrachlorethane poisoning, which is used in waterproofing the wings, etc.), together with a glossary of aviation terms and a complete bibliography of aviation medicine to date, complete this valuable book.

R. S. McC.

THE OPERATIVE STUDY OF GOITRE. THE AUTHOR'S OPERATION.
By WM. F. HALSTEAD. Johns Hopkins Hospital Reports., Vol. XIX, Fasciculus 2. Pp. 257; 11 plates. Baltimore: Johns Hopkins Press, 1919.

HERE is told the tale of the surgeon's struggle, through many decades, to deal successfully with goitre, his failures, his partial successes and his ultimate achievement, a tale culled from wide reading in many languages and a long, broad personal experience. While the book undoubtedly will remain the authentic reference work on the subject, we believe it will not attract the many readers who expect in a book of this sort an entertaining story easily read; the "story" is too disjointed, too much a patchwork for enjoyment as a story.

The author has carefully set down synopses of all known operated cases until 1883 except for the German-speaking countries whose cases are too numerous for tabulation. Probably the earliest operation was in 1596. Although Hedenus did six excisions in the early 19th century and spilled very little blood, lay and professional opinion was strongly against surgical interference except in most urgent cases of dyspnea, until as late as 1870. It was massive hemorrhage that first checked all surgical efforts. In 1845 the Italian Porta ligated both superior and inferior arteries to cause atrophy of the gland and in 1862 the American Cooper used mass ligatures to cause reduction by sloughing. In 1866 his fellow countryman, Warren Greene, did perhaps the most important work in hemostasis. With the control of hemorrhage, the discovery of anesthesia and the acceptance of Listerism, the three greatest problems of surgery were solved and it remained to learn that in operation was a cure for hyperthyroidism, that total extirpation of the gland was followed by hypothyroidism and often by tetany and vocal cord paralysis, and finally there were developed refinements in technique, in instruments, incisions, approach to the gland and in the surgery of the

gland that placed thyroid surgery on sure ground. The greatest strides in these matters were made between 1878 and 1883 by Billroth, von Bruns, Reverdin, Mikulicz and preëminently by Kocher. The book closes with a brief statement of the author's original and important contributions to the technic of thyroid surgery. J. A.

WAR NEUROSES AND SHELL-SHOCK. By FREDERICK W. MOTT, M.D., LL.D., F.R.S., F.R.C.P., Brevet Lieut.-Col., R.A.M.C.; Senior Neurologist to the Maudsley Neurological Clearing Hospital, London, England. Pp. 328; 3 original colored plates and 93 illustrations. London: Henry Frowde, Oxford University Press, 1919.

COLONEL MOTT has written many articles during the war dealing with nervous and mental disorders which he came in contact with in his army hospital services. In this volume he treats on the types, causation and treatment of the various forms of "war neuroses." His studies of actual shell-shock, resulting in death without external evidence of injury, are very well presented and illustrated. He differentiates "commotional" and "emotional" shock, and quotes several of the continental authors in support of his view. In the group of the psychoneuroses he found an acquired or inborn predisposition of emotivity in a high percentage of the cases. He believes that these men did not make good front-line material and that much expense and loss of man power could have been saved to the army had they been weeded out by a more thorough medical examination by the recruiting boards. He considers a neurosis as a subconscious defence reaction to an intolerable situation, and in support of his view states that most cases of war neuroses were not associated with external wounds, and, *vice versa*, that men with somatic wounds rarely developed neuroses.

As to the true psychoses of war the author states there are none and gives many excellent arguments and facts in support of this view. The types and frequency of psychoses correspond approximately to those of peace times.

The treatment as outlined is brief and exact, but leaves much to the imagination of the reader.

The one criticism of the book is the confusing way in which the author has assembled the whole. Had the presentation been systematic the book would be much easier to read and to understand.

As a whole the volume is one of the best that has been written dealing with the neurological problems arising in the recent war.

F. H. L.

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
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ST. AGNES AND NORTHEASTERN HOSPITALS.

War Wounds of the Joints.—DELREZ (*Arch. Méd. Belges*, May, 1919, p. 513) says that of 190 joint wounds treated within one year, 21 were infected and of these 16 involved the knee-joint. Under treatment he discusses only these 16. Five cases of purulent arthritis were treated without mobilization, the results being as follows: One was amputated with cure, 4 being resected. Two of the resected cases died and 2 were cured, with ankylosis. One of the 2 cured cases had a streptococcic septicemia after the resection. Of the cases treated by arthrotomy and mobilization there were 3 with staphylococcic serous arthritis in which there was complete cure, with total preservation of motion. In 4 cases of purulent streptococcic arthritis normal or very extensive motion was obtained. In an eighth case (streptococcic infection) death occurred on the tenth day from cardiopulmonary complications. In a ninth case with osteo-articular wound of the knee (streptococcic infection), osteo-articular wound of the elbow and multiple wounds of the soft parts the condition of the patient was so feeble as to call for amputation on the twenty-second day. In the tenth case (streptococcic) extensive destruction of muscles by gas gangrene rendered active mortification impossible. Prolonged efforts were followed by cure with partial mobility. In the eleventh case active mobilization was equally impossible, and, as in the previous case, passive mobilization was practised, so that after prolonged treatment and the help of an apparatus fair function was obtained. This (the Willems) method of treating joint infected wounds by active mobilization has furnished very satisfactory results.

Blood Transfusion as a Therapeutic Aid in Subacute Sepsis Associated with War Injuries.—ZINGHER (*The Military Surgeon*, 1919, xlv, 75) says that blood transfusions should be used more extensively on the wounded soldiers in the base hospitals. Officers should be especially

assigned to this work in the different base hospitals and base hospital centers, whose duties would be in connection with the performing of transfusions, consultations on medical and surgical cases and the keeping track of suitable donors. The special indications considered here are subacute sepsis, associated with extensive suppurations or with infected compound fractures, with anemia and emaciation of varying grades; also as a prophylactic measure in enfeebled individuals before severe operations and in cases of postoperative surgical shock resulting from extensive loss of blood during operation. Large pockets of pus, suppurating joints or extensive empyemas must, of course, be incised and drained. No blood transfusion will help in the elimination of these sources of continuous reinfection unless they are carefully watched for and taken care of as they arise. Autopsies often bring to light such complications, which should have been taken care of while the individual was still alive. The transfusions should be of moderate amounts of blood, from 250 to 300 c.c., and repeated, if necessary, every seven to fourteen days. Systematic efforts should be made to find these patients in the base hospitals. Special studies should be made and records kept after the transfusions, so as to obtain, as soon as possible, tabulated data that will help in more definitely indicating the value of blood transfusion in cases of subacute sepsis associated with extensive wounds and fractures.

Knee-joint War Injuries, with Report of 82 Cases Treated by Willems' Method.—McWILLIAMS and HETZEL (*Annals of Surgery*, 1919, lxx, 257) says that in the management of septic cases as soon as frank pus is evident, either by signs of inflammation or bacteriological examination, thorough drainage must at once be established by vertical external and internal incisions. The joint is washed out thoroughly with Dakin's solution at the time of operation. Tubes had preferably not be used at first but may be later, if drainage is found to be insufficient. When they are used, the internal ends should project just inside the synovial membrane and no further. The after-treatment is conducted exactly as in the case of non-infected joints by active (not passive) motions carried out to the point of pain. These are begun immediately after the anesthetic has worn off and are repeated every two hours thereafter day and night. Even a day's delay will prejudice the final functional result. Walking is important because the muscular contractions compress the joint and cause a marked increase in the expulsion of the pus. The patient is made to walk the next day after the operation without crutches. It is surprising how much pus will exude from the incisions after each walk. It is very important that sufficient drainage openings be made to allow for an adequate escape of pus. These openings should be sutured just as soon as the discharge becomes serous. If the active motions are performed often enough and vigorously enough, these secretions are expelled through the drainage openings as they are formed. Drainage seems to be more thoroughly accomplished by this method than by any other, thus limiting the infection to the synovial membrane and tending to prevent its spread to the cartilage and bones. In civil injuries the results of operations with débridement, joint closure and immediate subsequent mobilization should be much better than in war injuries, because the patient is operated on more quickly, the infection

is not so virulent, there is no transfer to another hospital, and, finally, the after-nursing should be more effectively done. He concludes that no joint injury should be evacuated within ten days after the operation. The joint should be completely closed at the operation. No splint should be used except in those cases where fragments will be displaced. The Willems after-treatment of immediate, continuous, active movements should be unceasingly kept up day and night both in the aseptic and septic cases. In each hospital there should be a day and a night nurse who should be conversant with the method and whose only function it should be to carry out the active motions.

Fracture of the Acetabulum with Intrapelvic Displacement of the Femoral Head.—PEET (*Annals of Surgery*, 1919, lxx, 296) says that this fracture with central dislocation of the femoral head has a high mortality and is fortunately rare. Depression of the trochanter and rectal palpation of the femoral head are important diagnostic signs, but every case should be roentgen-rayed. Complications are frequent, severe in nature and demand immediate recognition and treatment. The successful repair of the fracture dislocation depends much on its early diagnosis. Reduction by manipulation is recommended. Open operation is necessary only in the exceptional case or for the treatment of complications. Resection of the femoral head is unnecessary. Manipulation under general narcosis, when the dislocation is unreducible, has yielded excellent results in freedom of motion and capacity to use the leg.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Serofibrinous Pleurisy by Artificial Pneumothorax. WEIL (*Traitement des pleurésies sérofibrineuses par la pneumoséreuse thérapeutique* (*Bull. de l'acad. de Méd.*, 1919, lxxxi, 846) recommends injection of air into the pleural cavity after every puncture for serofibrinous pleurisy. The main benefit is that of preventing subsequent adhesions and the secondary difficulties that may develop. Of 86 cases of serofibrinous pleurisy subjected to puncture alone, 72, or 84 per cent., showed marked secondary trouble a few months or weeks later. Of 50 cases, on the other hand, in which puncture was followed by air injection 41, or 82 per cent., recovered without adhesions. In the 9 cases that did show pleural adhesions, the affection was of long standing before treatment was instituted. Seventeen cases out of the 50 treated with

injection of air recovered completely in from two to three months after a single injection. Fever and the other signs of infection rapidly disappeared, and most of the patients gained from 10 to 15 pounds in weight. A few recovered in less than a month. Thirty-three cases required more than one injection, but recovery, though more delayed, was as complete as in the cases requiring but a single injection. In cases where there is a rapidly recurring effusion, recovery is much delayed but this is possible after prolonged treatment. One such patient recovered in a year, having received in that time ten injections. One great advantage of the injection of air is that when pulmonary tuberculosis is the underlying cause of the pleural effusion, the effect of the induced pneumothorax is an arrest of the tuberculous process. It is most important to control such treatment by the roentgen ray and Weil's work was carefully controlled by radioscopy.

The Use of Benzyl Benzoate in Dysmenorrhea.—LITZENBERG (*Jour. Am. Med. Assn.*, 1919, lxxiii, 601) writes concerning the effect of benzyl benzoate in dysmenorrhea and reports inconclusive results regarding its value. He tried it in a series of 43 cases, in which 81.3 per cent. were relieved. Pain was absolutely eliminated in 62.7 per cent.; greatly relieved in 18.5 per cent.; slightly benefited in 4.6 per cent. These results, while not conclusive, warrant a more thorough test of the value of benzyl benzoate in dysmenorrhea. Benzyl benzoate is irritant when administered by mouth and should be given in capsules, well diluted with water, or as a 20 per cent. emulsion with acacia (this last preparation was found to be the most satisfactory). The dosage recommended by Macht proved insufficient, so Litzenberg finally increased the dose to 2 drams every two hours. No bad effects were observed, unless an occasional case of vomiting and rarely a feeling of weakness might be attributed to the drug.

A Therapeutic Study, Pharmacologic and Clinical, of Benzyl Benzoate.—MACHT (*Jour. Am. Med. Assn.*, 1919, lxxiii, 599) describes a number of clinical conditions that have been treated with benefit by benzyl benzoate. They may be summarized as follows: (1) Excessive peristalsis of the intestine, such as diarrhea and dysentery. Here, truly remarkable results were obtained; diarrheas of long standing were quickly checked and even dysentery was benefited by it. (2) Intestinal colic and enterospasm. (3) Pylorospasm, whether functional or reflexly produced by ulcers, etc. (4) Spastic constipation, in which there was a tonic spastic condition of the intestine. (5) Biliary colic. (6) Ureteral or renal colic. (7) Vesical spasm of the urinary bladder. (8) Spasmodic pains originating from the contractions of the seminal vesicles. (9) Uterine colic. (10) Arterial spasm, including a large number of cases of hypertension. The lowering of blood-pressure produced by benzyl benzoate was more lasting than that produced by administration of the nitrites. (11) Bronchial spasm. Wherever there were signs of bronchial constriction or spasm, benzyl therapy produced relief in almost every case. The theory of the action of benzyl benzoate is its relaxing effect upon spasms of smooth muscle tissue. The remedy was administered by mouth in doses of 25 minims of a 20 per cent. alcoholic solution—equivalent to 5 grains of the drug.

Vaccination by Subcutaneous Injection.—GOODALL (*Lancet*, 1919, No. 5007, p. 285) has vaccinated hypodermically over 6000 men. He uses ordinary vaccine, injecting 1 c.c. for each inoculation. The local reaction usually is manifest within two to four days. It is variable in intensity, and was very mild except in a small percentage of cases. He compares the local reaction obtained with that following anti-typhoid inoculation; that is, local swelling, heat, tenderness. In those cases showing marked reaction, there was swelling of the entire arm and hand with axillary involvement. After the seventh to the tenth day, the local swelling and induration subsides leaving a hard nodule in the subcutaneous tissues. This nodule becomes well circumscribed and usually lasts for about one month. The general symptoms vary in intensity and are very similar to those of ordinary vaccination. Goodall claims that the advantages of this method are that it is a clean surgical operation and there is no open wound and therefore dressings are not required. He states that with proper technic the danger of secondary infection is practically eliminated. He claims that the percentage of positive reactions is very high; only 8 per cent. of vaccinations proved ineffective. This method is painless as compared with the ordinary method of scarification; it is for this reason that he believes it the best method of vaccinating children.

PEDIATRICS

UNDER THE CHARGE OF

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The Artificial Feeding of Athreptic Infants.—MARRIOTT (*Arch. Ped. Proc. Sec. Dis. of Children, A.M.A.*, July, 1919) uses the term "athrepsia" in reference to that well known condition of extreme malnutrition known as marasmus or infantile atrophy. The condition of athrepsia is a condition of virtual starvation, in which the volume of the blood was diminished. This diminished flow of the blood was dependent in part at least upon a decreased blood volume, seemingly the result of a decreased protein content of the plasma and a consequent inability of the blood to maintain its water content. Very considerable amounts of food were indicated to meet this condition, yet the tolerance of many of these children for food was low and their digestion and absorption were necessarily poor. The tolerance of the infant for food might be increased by the use of gum acacia saline mixture intravenously. The problem remained of providing a food containing the elements essential to nutrition and which could be fed in large amounts without causing gastro-intestinal disturbances. In cases in which breast milk was not available, the use of lactic acid milk showed that it could be taken in larger quantities than sweet milk. Marriott came to regard buttermilk and protein milk as his chief reliance in feeding infants with gastro-intestinal disturbances. Fat-free lactic acid milk is low in caloric value. This might be increased by the

addition of sugar and starch, but even when enriched by sugar addition, it was not particularly adapted for the feeding of athreptic infants, particularly those under three months of age. There was no reason why the fat should all be removed from the lactic acid milk. In order to furnish the additional carbohydrate required by the athreptic infant, dextrins and glucose were added, the latter being absorbed with great rapidity. Glucose was very readily fermentable and for this reason was not used extensively in infant feeding. The dextrins, on the other hand, were not readily fermentable. It seemed that commercial glucose, being a mixture of dextrin, glucose and maltose might be suitable for the purpose. This is obtainable as corn syrup. Marriott added carbohydrate in the form of corn syrup to the whole lactic acid milk and used it in feeding athreptic infants. The results were as would have been expected. There was no tendency to diarrhea even when as much as 10 per cent. of the carbohydrate was added. There seemed to be almost no limit to the amount of carbohydrate that could be added to such a mixture. In addition a 5 per cent. solution might be given between feedings almost ad lib., as a means of supplying further calories. The thick syrup was rather inconvenient to handle, and could be best used in a solution containing 50 per cent. carbohydrate. As such a mixture was thick a nipple with a large hole had to be used in feeding. Up to the present time the author had fed forty infants varying in age from one and one-half months to eighteen months from periods of from four days to eight weeks. The amounts of carbohydrate added varied from 10 to 15 per cent. A gain in weight was noted in these children when a sufficient caloric intake was reached and generally continued steadily for days and weeks interrupted only by acute infections. Few infants, whose weight was as low as 50 per cent. of the normal weight for their age gained on less than 160 calories per kilo and many required 200 calories or more. The gain in weight in these infants was not due to a process of water logging. There was no tendency to edema and none of the excessive flabbiness observed in condensed milk babies. It might be noted that although the food described contained a high percentage of carbohydrates it was also high in protein and fat, the relative proportions being similar to those of ordinary milk mixtures. This mixture as described contained from 25 to 30 calories per ounce.

A Study of the Relationship of Convulsions in Infancy and Childhood to Epilepsy.—MORSE (*Am. Jour. Dis. Children*, August, 1919) recalls in this article the discussion of twenty or twenty-five years ago as to the connection between the convulsions of infancy and early childhood to epilepsy. Since that time he has made observations of the babies and children with convulsions that he has seen in consultation and in private practice. He includes in his observations only those cases in which the convulsions were the primary cause for calling in a medical attendant and he excludes all those cases in which there is any evidence of acute or chronic cerebral disease. This study was conducted with two objects. The first was to determine what proportion of the children, otherwise apparently normal, having convulsions have epilepsy or develop it later. The second was to find out if possible whether there is anything in the history or in the manner of development of the convulsions to show whether or not they are manifestations of epilepsy, or whether

they will be followed by or develop epilepsy later. Satisfactory reports regarding 107 children was obtained. The time elapsed has varied from two to twenty years. In order to study these cases they were divided into four classes: (1) Those having convulsions associated with spasmophilia; (2) those cases in which the convulsions occurred in the course of whooping-cough; (3) those in which there was a single convulsion or a series of convulsions at the onset of some acute disease or with an attack of acute indigestion; (4) those in which there had been repeated convulsions during a considerable period or in which there had been repeated attacks suggesting petit mal. The results of this study were most unsatisfactory and very few conclusions could be drawn from it. Convulsions, which are manifestations of spasmophilia, are not likely to eventuate in epilepsy. Convulsions which occur in the course of whooping-cough must always be regarded as serious, as they are likely to be followed by epilepsy later. Single convulsions or a series of convulsions occurring at the onset of an acute disease or with an attack of acute indigestion are less likely to be followed by epilepsy than are repeated attacks during a considerable period or repeated attacks suggesting petit mal. Repeated attacks which would be classified as petit mal, or which suggest it, are just as likely to become epilepsy as repeated attacks of general convulsions. Nothing can be told from the nature of the early attacks as to the nature of the attacks when the epilepsy develops. When an injury to the head has directly preceded the onset of the attacks or there is no apparent cause for the attacks, epilepsy is more probable than when there is an apparent cause, such as indigestion, for each attack. The presence of an apparent cause for the attack does not, however, exclude epilepsy. The longer the attacks have persisted the more probable is the diagnosis of epilepsy. General impressions, which cannot be explained, have a certain value in diagnosis. Finally, and most positively, there is no way to determine immediately when a baby or a child has a convulsion, or has had repeated convulsions, or repeated attacks suggesting petit mal, whether it has epilepsy or whether it will develop it later.

A Study of the Lactose, Fat and Protein Content of Women's Milk.—DENIS and TALBOT (*Am. Jour. Dis. Children*, August, 1919) give the results of their investigations of the composition of human milk under different conditions. They point out the fact that, while the limits and variations in the fat and protein content of human milk are well established, a great deal of uncertainty exists as to the amount of lactose present. This is due to the fact that while reliable and simple methods for the determination of fat and protein have been in use for many years, the technic for sugar determination is still complicated. Recently newer methods have been promulgated for the determination of lactose. In addition there has been introduced another simpler method of fat and protein determination so that it is possible now to determine accurately the quantity of fat, protein or lactose from small samples of milk. It was found that there is a rapid increase of lactose during the first few days when colostrum changes into milk, and a further increase as lactation progresses. The reverse is true of protein which after the first rapid decrease during the change from colostrum to milk tends to further decrease during the course of lactation. After

the colostrum period there does not seem to be any relation between the stage of lactation and the amount of fat in the milk. There is usually a higher percentage of lactose at the beginning of a single nursing than at the end. Although this difference may be one or more per cent., it is usually higher at the end of nursing than at the beginning. There is very little, if any, difference in the protein. The milks taken simultaneously from both breasts of the same woman tend to have the same composition, but often vary in respect to the percentage of fat. Toward the middle of the afternoon or later the volume of milk in a woman tends to diminish. The percentage of fat is as a rule higher at mid-day or mid-afternoon than at other times of the day.

OBSTETRICS

UNDER THE CHARGE OF

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The Puerperal Period Complicated by Sloughing Fibroid.—KOSMAK (*Am. Jour. Obst.*, March, 1919) records the case of a primipara admitted to the hospital at term with a history of bleeding for a few days. On examination the cervix was soft and boggy, with two fingers' dilatation, the membranes intact and vertex presentation of the fetus without engagement. A low implantation of the placenta was made, but there was little bleeding and the general condition was good. Labor progressed very slowly and the dilating bag was introduced and spontaneous delivery occurred. There was moderate hemorrhage during the third stage. Lacerations were repaired. After the birth of the child the patient was irrational and very restless for several days, and a tumor the size of a fibroid head could be outlined on the anterior wall of the uterus. There was considerable shock, and stimulation was needed for several days. A tear in the perineum sloughed without an attempt at union. Involution was very imperfect and the lower abdomen was tender. The lochial discharge was foul, but drainage seemed to be good. On the ninth day postpartum blood examination showed marked anemia, with hemoglobin 38 per cent. On the thirteenth day the patient complained of severe pain in the left lumbar region. Three days later she suddenly showed signs of a general peritonitis. The lower portion of the abdomen, with the tumor, was exceedingly tender. The symptoms pointed to a sloughing fibroid, with possible perforation. On internal examination the cervix was partially closed; there was no bulging behind the uterus and a very slight serous discharge. There was severe abdominal pain and great restlessness. The condition was so bad that it was thought advisable to wait until the following day, hoping that stimulants would bring about improvement. When section was done, seropurulent fluid escaped from the peritoneal cavity. The omentum was adherent to the top of the uterus, which contained the tumor. Perforation had occurred at a number of points through which purulent matter was exuded. The condition in the abdomen was that of diffuse

septic infection. Hysterectomy was performed as rapidly as possible. A stump of the cervix was left in the lower angle of the abdominal wound. The peritoneal incision was closed except at the lower angle, where a strip of iodoform gauze was passed down into the cul-de-sac. The patient was difficult to manage, refusing food, irrational and developing incontinence of the bladder and rectum, with beginning bed-sores. These were treated most successfully by exposing the tissues about them to the sunlight daily for several hours. There was a profuse genital discharge which persisted for some time. Thrombophlebitis of the left leg developed, but the patient gradually recovered and left the hospital in very fair condition. Examination of the material removed showed infection with the *Bacillus coli communis*. In discussing this paper several cases were reported of fatalities complicating pregnancy in which infection and sloughing developed. These cases were saved by hysterectomy, but it was thought that the operation should be done as early as possible.

The Technic of Salpingectomy in Ectopic Gestation.—CAREY (*Am. Jour. Obst.*, March, 1919) reports the case of a patient, aged thirty-nine years, admitted to the hospital with symptoms of ruptured ectopic pregnancy. At operation the left broad ligament was very much swollen, edematous and friable, and the tube was in the same condition. Abortion had taken place from the fimbriated end of the tube. The operator attempted to save a part of the tube and removed the outer half, leaving the ovary. After the patient's recovery she came for examination, when it was found there was a small, fixed, moderately tender mass on the left side of the uterus. The patient had a retroverted, prolapsed uterus, with old lacerations and cystocele, and on opening the abdomen the sigmoid and omentum were adherent in the region of the left tube and ovary, the part of the tube which had been left was atrophic and closed and the ovary had been replaced by a cyst a little larger than a golf-ball. The cyst was removed, the raw surface covered over and the uterus fixed to the anterior abdominal wall. The patient made a good recovery. The writer cites this case as illustrating the failure of his attempt to preserve a portion of the tube. He believes that a much better result would have been obtained had both tube and ovary been removed entire.

Contra-indications to the Use of Dilating Bags.—HULL (*Am. Jour. Obst.*, March, 1919) calls attention to several important contra-indications to the use of dilating bags. Before introducing the bag the operator should be sure that the cervix can be dilated and that there is good reason for believing that labor pains will develop. He must be on his guard against a rigid cervix and primary uterine inertia. In two cases the use of bags failed, although continuous traction was made with a two-pound weight. It was necessary to deliver these patients by vaginal Cæsarean section. Bags were also contra-indicated when great haste is necessary, as in severe accidental hemorrhage, threatened edema of the lungs and tightly contracted uterus or failure in cardiac compensation. In contracted pelvis with a true conjugate of less than 8 cm. the use of bags should not be permitted. In borderland cases induction of labor has been abandoned by the writer. He prefers to put the patient in the best possible condition and to give her the trial of labor,

watching closely the condition of mother and child. The results of induced labor in contracted pelvis are so much inferior to those of spontaneous labor or Cesarean section that induced labor should rarely be done. In complete placenta previa with viable child, section should be employed instead of the use of the bag. Virulent infection of the genital organs should contra-indicate the use of the bag. As regards normal cases at term it is difficult to find a good excuse for interference by the use of dilating bags. There is no way of determining the proper time for this operation. and the complications which may accompany the use of bags are sufficiently important to be avoided. When dystocia lies in the soft parts it is often preached that the bag is the ideal method of treatment. It is true that complete dilatation cannot be obtained, for the bag cannot imitate or set up the normal action of the uterus. The cervix is never completely dilated under the use of the bag alone. While it is true there are certain conditions in which the bag acts properly, its use has been greatly overdone, and it does not give the best results in many cases.

Cerebral Hemorrhage Complicating Pregnancy.—LANGROCK (*Am. Jour. Obst.*, March, 1919) describes the case of a primipara, aged twenty-three years, who had been feeling well until she had a convulsion and became unconscious, and up to the time of her admission to the hospital did not regain consciousness. The diagnosis of eclampsia had been made, and on admission the blood-pressure was 180 and the pulse 54. The patient had Cheyne-Stokes breathing and the respirations were very shallow. Only a few drops of highly colored urine were obtained by catheter. There was slight edema of the lungs, more marked of the ankles. The whole right side of the body was exceedingly spastic, and this was also true of the left lower extremity. The neck was slightly rigid, the left pupil widely dilated, the right contracted to a pin-point and neither reacted to light, nor was there corneal reflex. Babinski's sign was present on both sides, with exaggerated knee-jerks. There were moist rales through the lungs, while the heart sounds were feeble and very irregular. On abdominal examination the uterus was eight and one-half months; the head was freely movable above the pelvis. The fetal heart was heard very plainly in the left lower quadrant, beating 148 times to the minute. On vaginal examination the cervix admitted two fingers, and was soft and thin. Lumbar puncture was exceedingly difficult and only a few cubic centimeters of bloody fluid was obtained. The patient was not in labor, although the cervix showed two fingers' dilatation and was soft and thin. The diagnosis lay between eclampsia and intracranial pressure, and the latter seemed probable because of the unequal pupils, which did not react; slow pulse, Cheyne-Stokes breathing, spastic contraction of muscles and the Babinski reflex. The intracranial pressure was thought to be due to cerebral hemorrhage from eclampsia, injury to the cranium during her fall to the floor following the first convulsion or cerebral hemorrhage from a rupture of the bloodvessel, the seat of syphilitic endarteritis. At the moment of the patient's death, postmortem Cesarean section was done, and a child weighing six pounds and fourteen ounces, vigorous and in good condition, was delivered. The patient lived but a short time, dying from failure of the action of the heart, with profound cyanosis.

GYNECOLOGY

UNDER THE CHARGE OF

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Carcinoma of Ovarian Teratoma.—In view of the evident irritating character of the contained cyst fluid, together with the chronic irritation caused by the hair, producing as it does granulation tissue with giant-cell formation, it is remarkable that more cases of carcinomatous degeneration of the epithelial lining of teratomatous cysts, commonly called "dermoid cysts," of the ovary have not been observed. A possibility exists that too often these tumors are regarded as innocent and no gross or microscopic examination of the tumor is made as a matter of routine. In view of the skepticism usually expressed in commenting on carcinoma of the ovary arising from the epithelial lining of a cystic teratoma, the case recently reported by SPALDING (*Am. Jour. Obst.*, 1919, lxxx, 401) is of more than passing interest. The tumor was noted some days after operation following the laboratory routine which has to do with more pathology than the staff can promptly handle. It has taught the lesson, however, to cut all tumors grossly in the operating room and to have frozen sections made in suspicious cases before the abdomen is closed. In this case the tumor that was removed had all the appearances of an ordinary dermoid cyst, containing gelatinous fluid and red hair, but in addition there was a small nodule, yellow in color, which was resting on the cyst lining and which was surrounded by a narrow margin of ovarian tissue. Microscopic examination of this nodule showed a thin stratum of pavement epithelium with a distinct basement-cell layer. This epithelial layer varies in thickness and at one point gives the appearance of malignant change. The epithelial cells are increased in number at this point forming a small epithelial pearl which seems to be breaking through the basement-cell layer to invade the deeper tissues. Immediately beneath the epithelium is a layer of connective tissue and muscle cells which contain many sebaceous glands and several hair follicles. Several of these glands are invaded with epithelial cell masses resembling basal-cell carcinoma. Intermingled with the deeper layers of the connective tissue and extending to the fibrous capsule of the teratoma but not penetrating it is a carcinomatous mass forming in part solid masses of small, round epithelial cells surrounded by a scanty amount of connective tissue and in part small collections of epithelial cells having an alveolar arrangement. From this pathological picture it is very difficult to decide whether the process is an adenocarcinoma or a basement-cell carcinoma and whether the malignant tumor is primarily in the ovary or comes from a malignant

degeneration of the epithelial lining of the teratoma. In the year and a half that has elapsed since operation there has been no evidence of a recurrence, a fact uniquely at variance with the heretofore reported cases. This suggests the possibility that with early carcinoma the prognosis may be good because of the thick protecting capsule of the teratoma.

Secondary Syphilis of the Uterus.—Secondary syphilis of the uterus is seldom recognized and in the few cases that have been reported, the lesions have consisted of macules, papules and ulcerations located on the outside of the cervix. In a most interesting case reported by GELLHORN (*Surg., Gynec. and Obst.*, 1919, xxix, 374) the signs differed from this general picture in several important particulars. Whereas in all previously known cases the lesion was situated upon the outside of the vaginal portion, this is probably the first instance where the specific affection could be demonstrated within the cervical canal. This was possible because there was a marked eversion of the cervix which exposed the lower third of the cervical canal. The cervical mucosa showed posteriorly, an oblong patch, about $\frac{3}{4}$ cm. in its longest diameter, which lay about $\frac{1}{2}$ cm. from the external os. This patch was very slightly raised above the neighboring mucosa and had a finely granular, pinkish surface. At the circumference and extending a little into the patch was a faintly yellowish discoloration. Two other smaller and more nearly round patches lay to the right of the larger lesion, and a fourth patch could be seen upon the mucosa anteriorly. All these patches felt soft to the touch and bled very slightly when rubbed with a cotton-armed applicator. The secretions from these patches showed an abundance of very active spirochetes of the typical pallida variety. There were no secondary lesions anywhere on the body, and as the state of the primary lesion on the labium minus indicated the recent date of the infection, the intracervical ulcerations must be regarded as the first and only secondary manifestations of syphilis in this patient. Another important point that has been brought forward by this case has to do with the heretofore accepted view that the normal secretions of syphilitic women may cause infection even in the absence of local specific manifestations. In the light of the present observation, however, this conclusion may have to be modified, since the fortunate coincidence of a cervical tear permitted Gellhorn to inspect the inside of the cervical canal and to find there the specific lesions with their rich supply of spirochetes. It is permissible to assume that in all the previously reported cases in which syphilis was transmitted in the absence of any apparent lesions in the vagina or on the cervix, that such lesions existed within the cervical canal but were invisible through the closed external os. Until further evidence to the contrary is obtained, it will be safe to adhere to the old view that discharges contain spirochetes only in the presence of a local lesion.

Operation for Hypertrophic Elongation of the Cervix.—The operative procedure that has been suggested by NOBLE (*Am. Jour. Obst.*, 1919, lxxx, 409) for the correction of that interesting condition known as hypertrophic elongation of the cervix uteri, consists of resection of the

middle portion of the cervix supplemented by a shortening of the uterosacral ligaments by way of the vagina. The incision is made in the anterior median line of the vagina after the manner of a vaginal hysterectomy except that in place of encircling the cervix, the ends of the "Y" terminate at the side of the portio vaginalis. The bladder is liberated from the trigonum to the uterovesical peritoneum and laterally the dissection is extended outward along the base of the broad ligament to the ureter on either side and the peritoneum of Douglas's pouch is stripped free from the cervix up to the internal os. After liberating the neck of the uterus it is detached from the vagina by a V-shaped incision cutting from either side downward and toward the axis of the cervical canal. The incision should be made low enough to place the apex of the V at the vaginal junction. The resection is then completed by a similar incision immediately below the internal os, the effect of which produces a wedge-shaped stump of the uterus which will fit over the remaining cervical stump. At this point, the finger is passed into Douglas's pouch to locate the uterosacral ligament on the patient's left. Should it be completely effaced its markings may be located by drawing the uterus downward when a fold may be felt extending from the cervicocorporeal junction to the sacrum. With a pair of curved artery forceps thrust through the base of the broad ligament in the space between the uterus and the ureter (below the uterine artery) the fold or ligament is drawn well into the vagina and temporarily secured by a retention suture. The ligament on the opposite side is secured in like manner. Following this step the wedge stump of the uterus is secured in the V of the vaginal stump, first introducing a forceps or similar instrument through the vaginal portion and into the cavity of the uterus. Upon such an instrument the two sections are brought together and secured by a mattress suture of kangaroo tendon on either side, the two sections practically "dovetailing" into one another. To maintain perfect alignment of the canal a suture of catgut fixes the tip of the wedge into the angle of the V. By pulling upon the temporary retention sutures attached to the uterosacral ligaments, the latter will be drawn into the denuded field and tracing them step by step, using one pair of forceps after another, they may be brought far enough into the vagina to be sutured together in front of the cervix, the latter being forced well back into the hollow of the sacrum to secure normal fixation of the lower pole of the uterus. The excess of the vaginal flaps is then trimmed away and the vagina is closed with kangaroo tendon, the lower angles of the incision being left open for drainage. The edema of the vaginal portion which follows commonly disappears without attention but when the hypertrophy is due to inflammatory changes, wedge-shaped sections of anterior and posterior lips may be removed with good effect. On account of the relaxation of the vagina and its outlet, posterior colporrhaphy with especial attention to constructive reinforcement of the perineum is essential to effective employment of the mechanical principles involved in the technic of the operation.

OPHTHALMOLOGY

UNDER THE CHARGE OF
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Detachment of Retina in Toxemia of Pregnancy.—CLAPP (*Am. Jour. Ophthalm.*, July, 1919, p. 473) has examined the eyes of practically all of the albuminuria and toxemia cases occurring in the past fourteen years at the Maryland Lying-in Hospital, and has not observed detachment of the retina until recently. Six cases have presented themselves since December, 1917, whose histories are briefly detailed. They varied in extent from small to almost complete detachment of the retina, in contradistinction to so-called idiopathic detachments, these have all subsided and become reattached with normal fields of vision. They may be antepartum or postpartum, and may clear up in a few hours, and are frequently far forward in the periphery and found only after some searching. They are probably present much more frequently than heretofore recorded and the prognosis is good so far as the detachment is concerned.

The Eye of Birds.—ROCHON-DUVIGNEAUD (*Annal. d'oculist.*, June, 1919, p. 376) gives a résumé of the anatomy of the eye of birds. There are two types of eyes in birds: that of the diurnal with small cornea and large posterior segment, and that of the nocturnal with large cornea (and large crystalline) and relatively small posterior segment. The eye of diving birds presents certain peculiarities at the selero-corneal limbus: a kind of circular dilatation entirely surrounding the cornea. The crystalline of birds shows as its most important peculiarity an annular collar, the greater or less development of which according to different species modifies the form and consequently the refraction of the lens. The vitreous of birds is very consistent, which coupled with the bony scleral ring and the cartilaginous plate lining the entire sclerotic results in the posterior segment being very resistant, so that it is little or not at all affected by modifications of tension: the latter involves only the anterior chamber, very deep in the diurnal, still deeper in the nocturnal; the aqueous humor accordingly plays the essential part in the physiological maintenance and modifications of the intra-ocular tension. The pecten is nothing but a vascular membrane derived from the optic nerve, of which it represents the capillary network as a forward extension. It is an organ of nutrition to compensate the complete avascularity of the bird's retina; it has nothing to do with the accommodation. It is relegated to the postero-inferior segment of the eye, below and behind the foveal region so as not to interfere with the function of the latter. It is smaller in the nocturnal, probably because

the retina of these birds is relatively smaller than that of the diurnal. The ciliary muscle consists of three systems of striated fibers, the mechanism of which is incomprehensible with present theories of accommodation. The raptores, eagle, hawk, etc., possess actually two foveae, one central, the other further back (fovea lateralis). The central fovea is the principal one; its cellular layers (particularly the bipolar cells) are richer in elements. The posterior fovea is, however, well marked as a fovea: it is more or less developed according to the species. The eye of the eagle presents no difference, compared with that of other diurnal raptores except perhaps greater thickness of the osseous scleral plaques. Its axis is 27 mm. long with a maximum width of 32 mm.: it is accordingly larger and longer than the human eye; the retinal images of the eagle are therefore much larger than those of man—a circumstance favorable for visual acuity independent of all special function of the retina.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Occurrence of *Bacillus Influenzæ* in the Normal Throat.—

During the epidemic of influenza in October, 1918, PRITCHETT and STILLMAN found this organism present in 42 per cent. of 177 healthy individuals from whom no history or respiratory infection was obtainable. These observers found the same organism in the throats of convalescents from influenza in 46 per cent. of individuals studied. In the same epidemic period Lord, Scott and Nye demonstrated *B. influenzae* in the pharyngeal secretions of 76 per cent. of 34 healthy men of the Harvard S. A. T. C. Opie and his collaborators found *B. influenzae* in the mouths of 35.1 per cent. of all healthy men examined at Camp Funston. These figures indicate the wide distribution and prevalence of the organism during the severe epidemic of this acute respiratory disease. The authors (*Jour. Exper. Med.*, 1919, xxx, 497) made a study of the personnel of the Rockefeller Institute. Following up the examinations reported in their previous paper they have been able to make repeated cultural examinations of the throats of 84 of the same persons during a period of six months. The present study indicates that the percentage incidence of those harboring *B. influenzae* in the upper respiratory tract is as great during the post-epidemic period as it was during the influenza epidemic. From December, 1918, to June, 1919, the percentage of carriers in a group of 150 individuals has averaged 41 per cent. per month. This percentage incidence of healthy persons found to harbor influenza bacilli in their throats and saliva is approximately the same as that recorded by Pritchett and Stillman during the height of the epidemic. In addition it is of interest that in a boys' orphan asylum in which no case of influenza had occurred during

the epidemic 39 per cent. of throat cultures taken from 190 boys showed the presence of *B. influenzae*. This percentage incidence of positive cultures is the same as that found in the examination of 52 convalescents from influenza in an institution for girls in which over half the personnel had suffered from the disease. Healthy persons have been found to have positive throat cultures for a considerable period of time, in six instances during five months and in thirteen instances during a period of four months. The authors in every case used Avery's oleate hemoglobin agar. The optimum hydrogen ion concentration for this medium is shown to lie between pH 7.2 and 7.5. Any variation beyond this range, particularly on the alkaline side, reduces markedly the suitability of this medium for growth of *Bacillus influenzae*. Oleate hemoglobin agar not only enhances the growth of the influenza bacillus, but by inhibiting the growth of other organisms, such as streptococci and pneumococci, greatly facilitates the isolation of *Bacillus influenzae* from a focus which harbors a wide variety of other bacteria.

The Relationship of Proteolytic Enzymes in the Pneumonic Lung to Hydrogen Ion Concentration. An Explanation of Resolution.—LARD (*Jour. Exper. Med.*, 1919, xxx, 379) studied the effect of varying hydrogen ion concentration on the proteolytic activity of the cellular material of pneumonic lungs. This cellular material was the washed filtrate of finely ground lungs in the stage of grayish-red or gray hepatization and consisted mainly of pus cells, large mononuclear cells and pneumococci. In this he found evidence of the presence of a proteolytic enzyme which digested coagulated serum (Loeffler's blood serum, at a hydrogen ion concentration of pH 7.3 to pH 6.7). This enzyme was inactive at higher hydrogen ion concentrations. The pneumococci in the material had been killed by addition of chloroform. Also there was the presence of a proteolytic enzyme which was active between hydrogen ion concentration of pH 8 to pH 4.8. This was most active, however, at pH 6.3 to pH 5.2. He suggests that this enzyme action may be responsible for the dissolving of the exudate at resolution, *i. e.*, as a gradual increase in acidity occurs in the diseased lung the enzyme operative between pH 7.8 and pH 6.7 breaks down the fibrin. When a pH 6.7 is reached its action probably ceases and the action of the second enzymes continues, becoming very active between pH 6.3 and pH 5.2 splitting the peptones to amino-acid nitrogen.

Relations Between Pneumococci and Hydrogen Ion Concentration.—AVERY and CULLEN (*Jour. Exper. Med.*, 1919, xxx, 359) studied the hydrogen ion concentration at which bacterial growth of the various immunological types ceased, in an effort to determine if this method could be used for type determination. They obtained unsatisfactory results. Growth ceased with all types when a final hydrogen ion concentration of about pH 5 had been reached if sufficient fermentable carbohydrate was present in the culture media. Using dextrose this was found to be above 0.4 per cent. The same results were obtained using maltose, saccharose, lactose, galactose, raffinose and inulin. Excess of carbohydrate in the media up to 4 per cent. as tested did not influence this final reaction. They confirmed the results of Derby and Avery, that the optimum hydrogen ion concentration for growth

of the pneumococcus is pH 7.8. Where no carbohydrate was present other than that extracted from the meat as in plain broth, growth initiated at the optimum reaction of pH 7.8 ceased at about pH 7. If bacteria-free filtrates of such plain broth cultures were again readjusted to pH 7.8 and reinoculated the pneumococci could not grow unless carbohydrates were added. With such filtrates of dextrose broth cultures which had reached a final reaction, pH 5, growth occurred upon readjustment to pH 7.8 and reinoculation. Apparently one of the factors necessary for the growth of the pneumococcus is the presence of a certain amount of fermentable carbohydrate. LORD and NYE (*Jour. Exper. Med.*, 1919, xxx, 389) also found the final hydrogen ion concentration for growth of the pneumococcus to be about pH 5. There were no noteworthy differences with the various immunological types except in one instance when a strain of type I pneumococci remained alive for ten days after a hydrogen ion concentration in the culture media of pH 4.5 had been reached. They also found growth in dextrose broth cultures which had reached the final hydrogen ion concentration after readjusting the reaction and reinoculating. The strains of pneumococci tested withstood a hydrogen ion concentration of pH 5.3, one hour; pH 5.6, three hours; and pH 6.1, six hours before death of the organisms occurred. Cloudy suspensions of washed living pneumococci incubated with equal quantities of standard solutions of varying hydrogen ion concentration showed that there was no growth of the bacteria in tubes of pH 5.6 or higher concentrations after five and a half hours. In some of the tubes a clearing occurred due to dissolution or disintegration of the bacteria after seven hours. This was complete in such tubes of pH 5 to pH 6 only, the tubes on the more acid side remaining cloudy. There was constantly some clearing on the more alkaline side of the scale. They conjecture from this that the dissolution is not due to acidity alone as the more acid side of the scale remained cloudy and suggest that an enzyme derived from the pneumococci themselves active at pH 5 to pH 6 may be responsible. From these two studies it seems certain that fermentable carbohydrate must be present for the growth of pneumococci and that where this is present the production of acid is the most important bactericidal factor.

Experimental Streptococcic Tonsillitis.—In an attempt to ascertain the mode of dissemination and cause of influenza by the transference of secretions from the upper respiratory passage of influenza cases, to the nose and throat of healthy volunteer individuals, RICHEY (*Jour. Infect. Dis.*, 1919, xxv, 299) reports the production of tonsillitis in sixteen of 155 individuals who submitted themselves for the experimentation. Crude, unfiltered nasopharyngeal washings and bronchial secretions from acute typical cases of influenza were instilled into the nasopharynx of each volunteer. The usual incubation period was thirty-six to seventy-two hours. The predominating organisms in cultures from tonsils in early stages of the illness were hemolytic streptococci. Three of these cases had received one month previously a vaccine consisting of *Bacillus influenza*, pneumococcus, types I, II and III and *Streptococcus hemolyticus* in presumably adequate doses. A review of streptococcus vaccine therapy is given.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Observations on the Food of Anopheles Larvæ.—METZ (*Public Health Reports*, 1919, xxxiv, 1790) concludes an experimental study of the subject with the following discussion: It is evident from these experiments that the diet of Anopheles larvæ may be either heterogeneous or homogeneous—consisting of mixed animal and vegetable materials, of mixed vegetable materials or of individual species of plants or animals. And, apparently, it makes little difference whether the food is composed of living organisms or their dead remains. No effort was made to ascertain how many types of plants and animals furnish suitable food materials, since the range is evidently great. Only one of the types tested gave indications of being unsuited. This was Chara, and even it provided adequate food for the development of some larvæ to maturity. Of greater interest, perhaps, is the evidence regarding the effect of pollution or decomposition on the larval development. In most of the above experiments the culture media in which the Anopheles larvæ developed were essentially sterile, *i. e.*, there were practically no protozoa present and there was a negligible amount of bacterial action. The cultures were kept in shallow granite pans, 10 to 12 inches in diameter and 3 inches deep, and it was found that no artificial aëration was necessary. In other cases, when cultures containing relatively large amounts of decomposing vegetation were brought into the laboratory and kept without sterilization or aëration, the larvæ usually lost vigor and died in a few days. Thus the experimental evidence leaves little doubt as to the detrimental effects of pollution or decomposition. Whether the injurious effects of decomposition are due directly to bacterial or protozoal action on the larvæ themselves or indirectly to an excess of CO₂ or other gases resulting from the decomposition is not certain. The latter seems more probable, however, since the detrimental effects may often be prevented by aëration. Contrary to popular belief, then, it appears that the purer and more sterile the waters may be, so long as they contain sufficient food, the more suitable they are for Anopheles breeding. This would seem to account for the fact that rain-water puddles and seepage pools frequently permit much more prolific breeding than near-by, stagnant waters. It also serves to emphasize the danger of doing more harm than good by cleaning the refuse from such places as sloughs and stagnant puddles, unless adequate provision is made for subsequent drainage, oiling, fish control or some other method of mosquito eradication.

Observations on the Bacteriology of Influenza.—JORDAN (*Public Health Reports*, 1919, xxxiv, 1413) studied several groups of cases of influenza and other respiratory affections, with the object of ascertaining the frequency of Pfeiffer's bacillus, the Mather's diplostreptococcus and variations in bacterial flora throughout the illness. It was found that by ordinary bacteriological methods the flora varied markedly and that individuals of groups coming in intimate contact tend to a more or less uniform flora. In influenza Pfeiffer's bacillus and Mather's coccus occurred with greater frequency than other pathogenic organisms, and of the two mentioned Mather's organism seemed to be more frequently associated with pneumonia. In colds Pfeiffer's bacillus was relatively infrequent while Mather's coccus was present about as often as in influenza, and the latter organism was present in colds and rhinitis about as often as in influenza. Hemolytic streptococci appeared to be associated with tonsillitis and severe throat inflammation, while this organism was relatively rare in influenza. In the observations on "recurrences" of influenza, organisms different from those in the original attack were observed, and the opinion is expressed that "second attacks" are due to organisms different from those etiologically related to the first one.

Occurrence of Bacillus Botulinus in Nature.—BURKE (*Jour. Bacteriol.*, 1919, iv, 541) made 235 cultures from samples collected in five localities in central California, fifty or more miles distant from each other. The cultures covered a wide range of material, including tap water, hay, leaves, vegetables and fruits in various conditions, insects, spiders, sow bugs, snails, and caterpillars, garden soil, manure from horses, hogs, and chickens and also samples from the claws and beaks, and crop gizzard and intestinal contents of birds. Seven cultures of *Bacillus botulinus* were found in bruised and moldy cherries, bird-pecked cherries, pole bean leaf covered with spots or droppings of insects or small animals, spiders from bush bean plants, bush beans, some of which were slightly seared, picked over, washed and packed in clean jars for canning, manure from large hog which had recovered from botulism three months before sample was taken, and discolored moldy hay from an outdoor stack. Four cultures were found in which there was evidence of toxin, but it was so weak that the toxin-antitoxin tests were not considered reliable. This material was obtained from earth from spider tube, spider droppings and web, sow bug from bush bean plant, linnet claws, spider and small bugs from bush beans. Burke therefore concludes that *Bacillus botulinus* is widely distributed in nature, and that it is present in the garden and may be on the fruit or vegetables when they are picked. *Bacillus botulinus* is not necessarily associated with active decay. It may be present in the blemishes or spots on the skin of apparently sound fruit and vegetables. *Bacillus botulinus* may remain in the intestinal tract of an animal for at least four months after contaminated food has been eaten. *Bacillus botulinus* may not occur far from the habitation of man. Of the five localities visited, only one failed to give positive results as to the presence of *Bacillus botulinus*. There were no human beings living on the place, no domestic animals other than horses, and there was no vegetable garden. *Bacillus botulinus* may be closely associated with or dis-

seminated by spiders or insects common in gardens in California. Since *Bacillus botulinus* grows readily at temperatures as low as 22° C., there is no reason for assuming that this organism must be associated with the stools of warm-blooded animals.

The Diagnosis of Rabies in Animals.—HASSELTINE (*Public Health Reports*, 1919, xxxiv, 2378) describes his work and summarizes it as follows: The time required for the performance of the different tests is approximately as follows: Smear test: One hour (frequently less) after arrival of specimen. Section test: Three to four days (a hurried test can be done in a day but will usually be unsatisfactory). Animal inoculation test: Ten days to six months. After thirty days the probability of a positive result is small. In conclusion, therefore, it may be stated that, based on 1003 specimens examined, the correct diagnosis may be obtained on the day of receipt of specimen in 90 per cent. of the cases; within five days, in about 92 per cent.; and at the end of one month practically all will be determined. Hence a negative report on microscopic examination with subsequent inoculation of animals practically becomes a confirmed negative at the end of one month, though it is the rule at present to observe animals for six months.

Malaria in England in 1917 and 1918.—CARTER, of the U. S. Public Health Service (*Public Health Reports*, 1919, vol. xxxiv) reviews the recent outbreaks of malaria in England caused by the repatriation of large numbers of parasite-infected soldiers and emphasizes the unfavorable nature of the environment by pointing out that 15,000 imported cases gave rise to not more than 326 cases. The relatively small number of the mosquito hosts account for the failure of the disease to spread, though apparently the hosts are numerous enough to keep alive a small amount of infection even under ordinary conditions. It is predicted that the imported malaria will be of no importance in a year or two.

The Felix-Weil Reaction as a Laboratory Test in the Diagnosis of Typhus Fever.—BENGTSON (*Public Health Reports*, 1919, xxxiv, 2446) describes a relatively new diagnostic test for typhus fever. It depends on the agglutination of certain members of the proteus group with the serum from typhus cases. The method seems to be comparable with the Widal reaction in availability and it is in fairly general use where typhus prevails. The reaction appears in the first week of illness but is higher during the second week and during convalescence. A single positive result with a case of typhus of American origin is reported.

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ORIGINAL ARTICLES

ON THE EPIDEMIC ACUTE AND SUBACUTE NON-SUPPURATIVE
INFLAMMATIONS OF THE NERVOUS SYSTEM PREVALENT
IN THE UNITED STATES IN 1918-1919: ENCEPHALITIS;
ENCEPHALOMYELITIS; POLYNEURITIS; AND
MENINGO-ENCEPHALO-MYELO-
NEURITIS.¹

BY LEWELLYS F. BARKER, M.D., ERNEST S. CROSS, M.D.,

AND

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INTRODUCTION.

DURING 1918-19 there has been prevalent in the United States an epidemic disease, now known to be an inflammation of the nervous system, involving predominantly the brain (encephalitis), and sometimes the spinal cord (myelitis), but often involving both brain and cord (encephalomyelitis), or even including also to a certain extent the meninges and the peripheral nerves (meningo-encephalo-myele-neuritis). Observations of the disease in this country have been reported by K. A. Menninger, Peter Bassoe, Josephine B. Neal, O. L. Pothier, Beverley R. Tucker, Henry M. Thomas, E. W. Schnoor, W. E. Vest, H. Climenko, F. A. Ely, F. Kennedy, A. Gordon, B. Sachs, J. F. Shaw and F. H. Bartlett,

¹ This paper was presented (in abstract) before the Association of American Physicians at its meeting at Atlantic City, in June, 1919, and the abstract will be published in the Transactions of the Association.

F. Tilney and H. A. Riley, P. Wegeforth and J. B. Ayer, V. C. Vaughan, W. C. Allen, P. G. Woolley, I. Abrahamson, H. Belin, C. K. Mills and G. T. Wilson, C. A. Robinson, I. Strauss and S. Hirschfeld, J. A. McDonald, H. S. Howe, P. N. Bergeron, and K. H. Beall.

The epidemic in the United States must, we think, be looked upon as a part of a pandemic occurrence of the same disease, for epidemics closely resembling the outbreak here have been, since 1917, reported in many different parts of the world. The first outbreak to be observed in this pandemic seems to have been that occurring in Vienna in the winter of 1916-17. It was reported by von Economo, who called the malady, unfortunately perhaps, "Encephalitis lethargica." Another outbreak occurred in Australia, especially in Queensland and in New South Wales, in 1917, the "mysterious disease" having been reported in a paper by Breinl. In the spring of 1918 an epidemic of the same disease was recognized to exist in France, where Netter described it as *encéphalite lethargique épidémique*. Reports of the French epidemic have been made also by Sainton, de Saint Martin and Lhermitte, Audibert, Burger, Etienne, Miliam, Oliver, Claisse, and Claude and Schaeffer.

In March and April of the same year (1918) the malady appeared in epidemic form in fifty-one sanitary districts in England, especially in London, Birmingham, Sheffield and Leicester, and was reported by Harris, Hall, Batten and Still, Crookshank, Melland, Christopherson and Mawer, S. A. K. Wilson, E. F. Buzzard, S. K. Vaidya and others. The disease has also been observed in Africa, Ardindeteil reporting it in Algiers in 1918. In the latter part of 1917 and in 1918, cases were met with in Uruguay; they have been recorded by L. Morquio, of Montevideo. Several cases have been reported from Ireland by O'Carroll and Nesbitt (1919). Evidently, therefore, the outbreaks recorded in Europe, in Africa, in North America, in South America and in Australia indicate a world-wide distribution of encephalitis in epidemic form.

PERSONAL OBSERVATIONS.

Our own experience in the present epidemic dates from February, 1919; since that time we have had under personal observation several cases in which the diagnosis of acute or subacute encephalitis or encephalomyelitis has been made. Through the courtesy of Dr. H. M. Thomas, of Dr. John Howland and of Dr. Sydney R. Miller, who also have had a number of these patients under their care, we have been permitted to see several additional cases. On account of the great interest attaching to the subject, we shall in this article give the histories of several of the patients observed. In all these cases we have had the advantage of coöperative studies

made by a number of associates and colleagues; without their aid the data gathered would have, necessarily, been far from complete.

We desire to thank Dr. H. M. Thomas especially for much help in the study of these cases and Dr. Sydney R. Miller and Dr. Walter A. Baetjer for their painstaking laboratory examinations. We trust that the records here presented may, for purposes of comparison, prove helpful to others who have been studying the disease in the United States.

CASE I.—Male, aged twenty-seven years; single; clerical worker; seen February 20, 1919. Referred to office for diagnostic study by Dr. E. R. Dibble, of Marion, S. C.

Complaint. Drooping of eyelids; cannot move upper lip; food accumulates between teeth and cheek; difficulty in swallowing liquids.

Anamnesis (Summary). Healthy until present illness, except for an attack of amebic dysentery a year and a half ago and "influenza," followed by diarrhea, twelve weeks ago. Family history practically negative. Smokes ten to fifteen cigarettes a day. Does not use tobacco otherwise, alcohol or drugs.

Three weeks before he was seen he began to see double. At first the diplopia was absent for a short time each morning, but after a few days it became permanent. At about the same time he developed a facial paralysis on the right side, with ptosis and a weak lateral rectus of the right eye. The paralysis of the face extended slowly downward on the right, involving the parts around the lips and under the chin, after which it extended to the left side of the face.

Physical Examination (Dr. Cross). (Summary). Patient is about twenty-five pounds below his calculated ideal weight. He is rather pale. Tongue protrudes in midline; a little tremulous. Tags of tonsils on both sides. Superior maxillary arch contracted; moderate amount of dentistry; one or two teeth missing. Small thyroid struma. Slight general lymph-glandular enlargement. Pulse 27 to the quarter; regular in force and rhythm; vessel wall distinctly thickened. Definite fine tremor of the right hand; slight tremor of the left. Blood-pressure: 126 systolic; 80 diastolic. Triangular crines; abundant hairs; definite hypotrichosis of trunk. Both eyelids droop a little—the right more than the left. Neither can be closed tightly. The right eye will not follow the finger to the right; otherwise the eye muscles balance fairly well. The right pupil is much larger than the left; it reacts very sluggishly to light. The left pupil is about normal in size; it reacts fairly well to light. The patient is not able to wrinkle the forehead; lifts eyelids very little; apathetic look; is not able to show his teeth (Fig. 1). Knee-jerks present and about equal. Babinski negative, both right and left. Abdominal reflexes very active. Arm-jerks present. Jaw-jerk definitely a little exaggerated.

Laboratory Reports in Case I.

<i>Blood examination.</i>		No.	Per cent.
Red blood cells . . .	5,212,000	Polymorphonuclear neutrophiles	155 62.0
White blood cells . . .	6,200	Polymorphonuclear eosinophiles	5 2.6
Hemoglobin . . .	90 per cent.	Polymorphonuclear basophiles	1 .4
Red blood cells and platelets normal.		Small mononuclears	56 23.2
No abnormal cells seen.		Large mononuclears	31 12.4
		Transitionals	
			250 100.0

Blood Wassermann Reaction. Antigen (a) cholesterinized human heart, negative. (b) Acetone insoluble lipoids, negative; (c) plain extract of beef heart, negative.

Cerebrospinal Fluid Examination. Wassermann negative, with antigens (a) (b) (c). Cell count, 30. Small mononuclears. Globulin, ++++. Patient anesthetic to puncture.

<i>Gastric contents.</i> 80 c.c. recovered; colorless.	
Free HCl	48.0 acidity per cent.
Combined acid	23.0 acidity per cent.
Total acidity	71.0 acidity per cent.
Ocult blood	0
Lactic acid	0
Microscopically, negative.	

Stool Examination. Brown; formed.

Bile, +

Ocult blood, 0.

Microscopically, negative.

Urine Examination.

Reaction acid	Night	Day.
Specific gravity	1014	1006
Albumin	0	0
Sugar	0	0
Acetone	0	0
Microscopically: Few white blood cells, no red blood cells, no casts.		
Bile	0	0
Blood	0	0
Indican	0	0

Röntgen-ray Reports in Case I. Röntgenoscopic of Chest. Heart of pendulous type; aorta not remarkable. Retrocardial space clear. Lungs and diaphragm negative.

Röntgenoscopic of Gastro-intestinal Tract. Impression, functioning normally.

Röntgenogram of Paranasal Sinuses. Clear.

Röntgenogram of Lungs. A good deal of very fine mottling throughout. Increased fibrosis along the right mediastinal margin, extending up under the right clavicle. Apices relatively clear.

Plate suggestive of slight changes in right lung, as if there had been slight old infection. No fluid present in pleural cavities.

Neurological Examination (Dr. H. M. Thomas). Weakness of the external eye muscles, particularly of the right lateral rectus. Pupils are unequal and the reaction seems to be somewhat sluggish. The patient has partial paralysis of the right fifth nerve and of both seventh nerves. No observable disturbance of sensation. Patient's face has a peculiar set, expressionless look. No spontaneous twitching. Patient elevates the left eyebrow more than the right. Neither is raised as much as it should be. He can wrinkle the forehead scarcely at all. Neither eye can be closed completely. On attempting to elevate the lip there is slight contraction on both sides, but very little movement. Can just begin to pucker the lips. Faradic stimulation of the right facial muscles causes active contraction in the muscles supplied by all the branches of the right facial nerve. The same is true on the left side. With the galvanic current the muscles also contract strongly. Soft palate and tongue normal. Hearing normal. Station and gait normal. Deep reflexes somewhat over-active.

Dental Examination (Dr. H. H. Streett). Mastication much impaired from loss of posterior teeth. Number of cavities to be filled. Superior arch contracted. Roentgenograms negative.

REARRANGEMENT OF THE DATA IN CASE I.

CASE I (No. 5310). Male; aged twenty-seven years; clerk.

Complaint. Drooping eyelids. Loss of motion in upper lip. Difficulty in swallowing fluids.

Habits. Smokes ten to fifteen cigarettes a day.

Previous Infections. Amebic dysentery eighteen months ago. Influenza twelve weeks ago, followed by diarrhea.

Operations: 0. *Traumata:* 0.

Respiratory System. Tags of tonsils. Lungs negative. Roentgenogram of paranasals negative. Roentgenogram of lungs shows fine spotting in both lungs. More fibrosis on the right.

Circulatory System. Tachycardia, pulse, 108; radials thickened. Blood-pressure $\frac{120}{90}$. Heart negative.

Blood and Hemopoietic System. Red blood cells, 5,212,000; hemoglobin, 90 per cent.; white blood cells, 6200. Wassermann reaction negative (3 antigens). Polymorphonuclear neutrophiles, 62 per cent.; polymorphonuclear eosinophiles, 2.8 per cent.; small mononuclears, 23.2 per cent.; large mononuclears, 12.4 per cent. Slight general lymph-glandular enlargement.

Digestive System. Gastric Analysis. Free hydrochloric acid, 48; total acidity, 71; occult blood negative. Stool negative. Contracted superior arch. Moderate amount of dentistry. One gold cap. Roentgenograms of gastro-intestinal tract negative.

Dentist's report: Infection negative; loss of posterior teeth; cavities, 1.

Urogenital System. Urine: specific gravity, 1006-1014; albumin, negative; sugar, negative; casts, negative; white blood cells, few; red blood cells, none. Nycturia, 1-2.

Locomotor System. Negative.

Nervous System. Three weeks ago first transitory, then continuous, double vision, lasting two or three days. Cannot move upper lip. Food accumulates between teeth and cheek. Difficulty in swallowing fluids. No drooling. Ptosis both right and left. Lids cannot be closed tightly. Right lateral rectus weak; right pupil larger than left; right pupil more sluggish. Cannot wrinkle forehead nor show teeth. Reflexes, ++. Jaw-jerk, +++.

(H. M. T.). Weak right lateral rectus; anisocoria; sluggish pupils; partial paralysis of right fifth nerve and of both seventh nerves; suggests lethargic encephalitis.

Examination of Cerebrospinal Fluid. Clear; cells, 30; small mononuclears; globulin, ++++; Wassermann reaction, negative.

Metabolism and Endocrine Systems. Twenty-five pounds under weight. Small struma. Definite tremor of right hand and slight tremor of left.

DIAGNOSTIC SUMMARY OF CASE I.

1. Poli-encephalitis acuta superior et inferior, with slight meningeal irritation. (The case is possibly one of postinfluenzal origin and resembles very much the cases described of late as *encephalitis lethargica*.) There is bilateral ophthalmoplegia and also paralysis involving the right fifth and the right and left seventh, and slightly, the tenth cerebral nerve; the cerebrospinal fluid contains thirty small mononuclear cells and globulin.

2. Gastric hyperacidity.

3. Dental caries.

4. Undernutrition to a degree of about twenty-five pounds.

DISCUSSION OF CASE I. The localization of the pathological process in the nervous system in this case, at least so far as the chief symptoms and signs are concerned, was easy. The bilateral ophthalmoplegia, the dysphagia on the right, the bilateral facial paralysis, the dysphagia, and the persistent tachycardia pointed to the gray matter in the midbrain, pons and medulla oblongata containing the nuclei of origin of the III, V, VI, VII, IX (?) and X cerebral nerves, the lesions evidently being more extensive on the right than on the left side. Though there was very slight meningeal irritation (shown by the cell count and the globulin in the cerebrospinal fluid), there was no other evidence to support the view that the paralysis of the cerebral nerves was radicular rather than nuclear; indeed, the absence of any outspoken meningitis and of any symptoms referable to the hypothalamus, the basis pedunculi, the pars basilaris pontis

or the pyramids of the medulla seemed to rule out such radicular involvement. The lesions were evidently in the gray matter of the floor of the aquæductus cerebri (Nucleus n. oculomotorii); and of the floor of the ventriculus quartus (Nucleus [motorius] n. trigemini; Nucleus N. abducentis dext.; Nuclei nn. faciales; and, possibly, Nucleus ambiguus).

The nature of the pathological process we regarded as inflammatory (polioencephalitis acuta superior et inferior with slight myelitis bulbi and slight meningitis), for the mode of onset and course were against apoplexy, thrombosis, and neoplasm.



FIG. 1.—Case I as seen February 20, 1919. Ophthalmoplegia externa et interna; paralysis N. VII, bilateral; paralysis masseter (right); dysphagia; facial mask. (Midbrain; pons.)

As to the etiology of the inflammation, we ruled out lues by the Wassermann test of the blood and cerebrospinal fluid. The absence of tubercle bacilli, of pneumococci, of meningococci and of other bacteria from the cerebrospinal fluid was against infection by these agents. The cell-count in the fluid and the white count in the blood as well as the onset and course of the paralyses did not support the view that we were dealing with an unusual form of the Heine-Medin disease. Recalling the reports from Europe of the prevalence there of epidemic encephalitis, the probability of diagnosis of this disease was then made. Very soon we saw a number of other cases that confirmed this view.

CASE II.—Male; aged forty-six years; married; business man. Referred to office for general diagnostic study by Dr. M. E. Hundley, of Martinsville, Virginia, February 28, 1919.

Complaints. Pain in the head and neck, nervousness, emotionalism, weakness and aching in the legs, insomnia, forgetfulness, irritability and difficulty in walking, all dating from about the middle of November, 1918, just after a period when he had been caring for his family sick of influenza.

Anamnesis (Summary). *Family History.* Father died of arteriosclerosis at seventy-six, having had coarse tremor in both hands for forty years before his death, making handwriting impossible, though there were no movements of the head or disturbance of speech; mother living and well; one brother died of pulmonary tuberculosis; one sister has myocardial disease; wife has had one miscarriage. Patient has had nine children, all healthy.

Personal History. Patient had the ordinary childhood infections as well as typhoid; gonorrhoea at sixteen; denies lues. At one period he drank hard for eight or nine years, but he has used no alcohol for the past seven or eight years until recently, when he took some on account of insomnia. He has used much tobacco and chews all the time when he is well. He has worked in a room in which tobacco is steamed for ten hours a day for fifteen years. He has taken no vacation in the past fourteen years. For the last six or eight years he has carried strychnin tablets in his pocket, and when he felt let down he would take $\frac{1}{30}$ or $\frac{1}{60}$ grain. He thinks that he averaged an intake of about one dozen strychnin tablets per week.

When asked more in detail about his drinking habits he stated that he drank whisky heavily at about the age of thirty-two. He drank "for the effect," as it stimulated him both mentally and physically. He preferred good whisky and beer, averaging from four to six bottles of beer a day on "beer days" and about $\frac{3}{4}$ pint of whisky on "whisky days." Often he would drink twelve bottles of beer or one quart of whisky in a day. In spite of this he was always able to conduct his business. During ten years of such drinking his weight increased to 195 pounds and his blood-pressure became very high. He often had headaches and he felt badly in the mornings, but he worked hard, and, aside from his work, was well known as a successful local politician.

At the age of forty-two he stopped drinking whisky on his doctor's advice and took no more until the present illness. After stopping drinking his nervousness increased and he says that he became more easily excited and more irritable. His sons, who were rather wild, also worried him at this period. He found that he fatigued more readily than earlier in his life. There were days when he would be very tired and very depressed. In 1918, one son went to France, and this was an additional worry that bothered him greatly.

Present Illness. The patient dates this as beginning about the middle of November, 1918, when he became much more nervous and irritable, lost his temper very easily, became progressively weaker and suffered from aching pains in the legs. The depression

was at this time very hard to bear, and he was constantly tired and sleepy. He "could fall asleep at any time of the day."

During the month preceding the onset of his present illness he had greatly overtaxed himself caring for several members of his family who suffered from influenza. His wife had pneumonia and six of the children had influenzal attacks. The patient, however, during this time remained apparently well, nursing all of the family at night, with only snatches of sleep, and working at his business all day. He states that he chewed tobacco all day and all night, in order to keep awake. He also took a tablet of strychnin every three or four hours, either $\frac{1}{30}$ or $\frac{1}{60}$ grain.

The symptoms noticed at the onset continued to be manifest for several weeks, increasing all the time, until in February he had to give up his work. He noticed that he became very forgetful, had difficulty in locomotion, having to keep his eyes on the ground when walking. He had a dull, heavy feeling in the head and he developed marked tremor of the hands. Two weeks before coming to Baltimore for study he began to be very sleepless. His physician stated that he had had tachycardia recently. The patient complained that his eyesight had become poor and that "reading made his head swim."

Physical Examination (Dr. A. D. Atkinson and Dr. Barker).
Summary. Patient looks anxious and depressed. Fairly well nourished. Muscles flabby. Looks as though he had lost weight. Hair coarse and dry. Ears and mastoids negative. Pupils a little dilated, left larger than the right; right pupil reacts better to light than the left, though both pupils are rather sluggish on light stimulation and on accommodation. No nystagmus. Teeth suspicious. Tongue protrudes in the middle line. External ocular movements seem normal. Tonsils embedded and adherent. Cervical glands not enlarged. Slight enlargement of the thyroid. Some retro-manubrial dulness. Lungs negative.

Radial pulse 26 to the quarter. Blood-pressure: 190 systolic, 120 diastolic. Vessel wall palpable. Heart slightly enlarged, no murmurs. Abdomen negative. External genitalia normal. Deep reflexes sluggish, the right knee-kick being somewhat less active than the left. Gait a little disturbed when walking with the eyes shut. Finger-nose test and heel-knee test well performed. Rather marked coarse general tremor of the head and trunk. Some finer tremor of the fingers when the arms are extended. Prostate somewhat enlarged and firmer than normal; not tender.

Roentgenological Findings. Roentgenoscopic of cardiovascular stripe: Negative except for somewhat transverse position of the heart.

Roentgenoscopic Examination of Gastro-intestinal Tract: Normal findings.

Teleroentgenogram: M. R., 3.4; M. L., 10.4. Heart somewhat transverse in position. Aorta slightly dilated.

Rocntgenogram of Paranasal Sinuses. Both antra somewhat hazy, probably old infection.

Reports of Laboratory Tests. *Blood*. Red blood cells, 5,536,000; hemoglobin, 95 per cent.; white blood cells, 12,800; polymorphonuclears, 87.2 per cent.; polymorphonuclear eosinophiles, 0; polymorphonuclear basophiles, 0; small mononuclears, 9.6 per cent.; large mononuclears and transitionals, 3.2 per cent. Platelets normal. Wassermann reaction in the blood negative.

Gastric Contents. Free HCl, 10 acidity per cent. Combined acid, 34 acidity per cent. Total acidity, 44 acidity per cent. Some occult blood present with both the benzidine and the guaiac tests. Lactic acid, negative. Microscopically, negative.

Feces. Soft and liquid. Negative findings.

Urine. Negative except for a slight trace of albumin and a few white corpuscles.

Cerebrospinal Fluid. Clear; colorless; pressure increased; cell count, 11; small mononuclears. Globulin 4 plus; Wassermann, negative.

Dental Report (Dr. H. H. Streett). General condition of the mouth very bad. Mastication impaired from loss of posterior teeth. Teeth badly abraded and quite sensitive. A number of cavities open to the secretions of the mouth.

Roentgenographic review shows areas of rarefaction about the apices of the superior right first molar No. 3 and central incisor No. 8. As the conditions about these teeth could be foci of infection, they should be extracted and the sockets should be curetted.

Psychiatric Report (Dr. Adolf Meyer). "The patient apparently shows much less well-marked symptoms than he did a week ago. He does not feel depressed; is not uneasy or afraid; shows excellent memory in the usual tests; good grasp of a test story; fair retention. Early in February, however, he had a pronounced depression, with tearfulness easily elicited. He felt he was going to die; he worried about past indiscretions.

As to his physical status the tremor of head and of the hands, with a history of walking with extremely fixed attitude, and with the tendency to loss of balance, either forward or backward, suggests the possibility of an incipient Parkinsonian syndrome.

My impression is that the patient is recovering from a well-marked reactive depression. The important etiological factors are the strenuous work of the last fourteen years and the recent strain during the influenza epidemic, associated with cerebral arteriosclerosis, and the history of an earlier prolonged period of excessive alcoholism."

Diagnosis. Before the report on the cerebrospinal fluid came in we had not thought of the possibility of the existence of epidemic

encephalitis in this patient. Bearing in mind the long history of overstimulation (alcohol, tobacco, strychnin), of excessive application to work and of great family strain, together with the history of arteriosclerosis and marked arterial hypertension, we thought the condition could be explained upon the ground of an atherosclerosis, with chronic renal, cerebral, aortic and cardiac disease. The blood-pressure was 190 systolic and 120 diastolic. He evidently also had oral sepsis. As there was an outspoken facial mask, coarse tremor, a tendency to rigidity of attitude and to loss of balance, we thought that he was suffering from Parkinson's disease, probably due to arteriosclerotic lesions in the globus pallidus. There was a well-marked depression that we looked upon as reactive. He had also signs of a slight thyreopathy.

As the patient had to return home he was advised to have the oral sepsis corrected immediately and to go on a careful dietetic-hygienic regimen, under the supervision of his home physician, and to report to us later on.

Course. The patient stayed at home until May 1, 1919. During the first week or two he improved somewhat, but then rapidly became more nervous, could not lie quiet, had no appetite, and could not sleep. He suffered from "terrible depression" and was very emotional. At this time he started again to take some whisky, but he felt that it did him no good. His physician advised him to return to Baltimore, where he entered a nursing home, had a special nurse, was isolated, was kept in bed at first, and was given injections of cacodylate of soda, massage and a suitable diet. To our surprise the symptoms improved rapidly; the Parkinsonian mask quickly disappeared; the tremor became much less; the depression passed off; the patient resumed a much more normal behavior and his mood became more cheerful.

The following note on the physical condition was made on July 12, 1919, by Dr. M. C. Pincoffs. "Weight stripped, 159 pounds. There has been a distinct decrease in the loss of expressive movements and in the mask-like expression; the patient now laughs readily; there is now no crying even when subjects that formerly would have caused this were brought up. There is still rapid blinking of the eyelids. The eyes, roughly tested with types, show no diminution of vision. Extra-ocular movements normal. No definite von Graefe. There is a marked collar of erythema at the base of the neck and a distinct fulness in the suprasternal fossa. Most of this is a pad of fat, but the isthmus of the thyroid is distinctly thickened, and both lateral lobes of the thyroid are slightly enlarged. The apex-beat of the heart is just lateral from the midclavicular line; the right border is just to the right of the sternal margin. There is a distinct increase in the retrosternal dulness. Heart sounds clear. Rhythm regular. Radials are not thickened on palpation. Pulse-rate 100. Blood-pressure, $\frac{1}{1} \frac{5}{0} \frac{0}{0}$.

The liver margin descends several finger breadths below the costal margin. It is smooth, has rather a firm edge, and is somewhat sensitive. The rather coarse fluttering tremor of the hands formerly present has almost entirely disappeared. There is a persistent fine tremor at present. Knee-kicks active and equal. Biceps reflexes equal. Superficial abdominal reflexes hyperactive and equal. Dermatographia marked.

Impression. (1) The signs of hyperthyroidism of moderate degree are rather predominant in the picture at present. (2) There is well-marked tachycardia, slight dyspnea on exertion and occasional sense of suffocation. The blood-pressure is very labile— $\frac{1}{1} \frac{2}{2} \frac{0}{0}$ in February, $\frac{1}{9} \frac{4}{0}$ in bed, $\frac{1}{1} \frac{5}{0} \frac{0}{0}$ now when resting and $\frac{1}{1} \frac{7}{1} \frac{0}{0}$ on climbing stairs a few days ago. (3) The mental condition is very much improved, the depression and psychomotor retardation so evident at first have largely disappeared. But there is still evidence of an anxiety neurosis and the patient requires constant reassurance.

One might suppose that the encephalitis epidemica had been, in this case, an acute episode in a patient already affected by the results of overwork, chronic alcoholism, chronic tabagism and hyperthyroidism, and that we are now seeing the residual condition with the hyperthyroidism perhaps more prominent than earlier in the course.'

DISCUSSION OF CASE II. The occurrence of asthenia, drowsiness increased nervousness, emotionalism, mental depression and the signs of Parkinson's disease (facial mask; coarse tremor) did not at first call up the idea of epidemic encephalitis in this patient, owing probably to the fact that he had (1) an outspoken atherosclerosis with high blood-pressure, (2) oral sepsis, (3) a history of great strain and fatigue and (4) a long history of overstimulation (alcoholism; tabagism; strychninism). It was the findings in the cerebrospinal fluid that first suggested the superimposition of an epidemic encephalitis upon his other maladies, and a careful consideration of the date of the disease, the conditions and mode of onset, the symptoms and the course, has confirmed us in the opinion that the patient was really infected with the virus of epidemic encephalitis. A striking feature of this case, as in Case III, is the long history of chronic alcoholism. That chronic potatorium predisposes to encephalitis and especially to poli-encephalitis superior has long been known. Indeed, Wernicke's type of encephalitis is sometimes referred to as the "acute ophthalmoplegia of drunkards." In our Case II, the process seems to have affected (1) the cortex (amnesia; stupor and later insomnia; depression), (2) the globus pallidus (Parkinsonian syndrome), (3) and, slightly, the midbrain (pupillary changes). He is making a satisfactory recovery.

CASE III.—Male; aged forty-eight years; married. Referred for diagnostic study by Dr. W. W. Stewart, of Columbus, Georgia, and by Dr. Allen of Oswitchee, Alabama. Admitted to private ward in

Johns Hopkins Hospital, March 3, 1919. Discharged, April 30, 1919. (No. 5599.) Patient was unable to give a correct statement in regard to his condition, and the history was given partly by his sister, partly by the letters from his physicians at home.

Complaint. Pain in back of neck and head.

Family History. Father died, aged sixty-two years, of softening of brain; otherwise negative.

Personal History. General health always good. No serious illness at any time. Alcoholic for many years, but has drunk less during the last year. Relative told his nurse that for the last ten years he has averaged about one quart of whisky every night! Heavy smoker for a number of years.

Present Illness. About January 21, 1919, the patient felt suddenly weak all over. Pain in back of head, so severe at times that he would grasp his head in his hands and cry out. Mind immediately became affected. Memory was impaired and there was lack of coherence in his talk. No convulsive attacks nor loss of consciousness at any time. Rational periods alternated with periods of delirium. Two days before he was seen he had threatened to commit suicide all of one day. For a few days after onset of illness the face and head "would draw toward the right;" the arms were stiff and were flexed medialward across the chest. For the last eight months he has had sulky spells, and for the same length of time he has been easily irritated and often became angry with members of his family without real cause. His temperature on the first day of his illness was 104° , but it gradually came down to normal on the fourth day. On the sixth day he had numerous "blisters" around the nose and mouth (herpes?). The physician consulted at the onset of his illness knew of the chronic alcoholism, found albumin and casts in the urine and made a probability-diagnosis of uremia (especially as there had been progressively increasing feebleness, rapid loss of weight and mental disturbance at times) and treated the case accordingly.

Physical Examinations (Drs. Barker, Irwin and Ward). The patient looks drowsy and toxic, though when spoken to he answers promptly. Face covered with small pitted scars, resembling those of smallpox. Muscles of mastication and of expression act well and equally. Tenderness on pressure over the entire cranium. No special tenderness over the temporal areas. The left pupil is a little irregular; both pupils react to light and to accommodation, but sluggishly. There are a few small superficial ulcers over the cornea on the left side. Von Graefe's sign is positive. Rosenbach's sign is positive. External ocular movements good. No nystagmus. Slight nasal obstruction on the right side. Marked auditory impairment on the right. Tongue is protruded in the midline; brownish coat; slight tremor. Throat injected; uvula pulled over to right side. Tonsils small; not injected. Gums show active pyorrhea; some dental caries; a good deal of dentistry. No general glandular enlargement. Thyroid not enlarged. Inconstant dry

râles throughout both lungs. Lungs otherwise clear on auscultation and percussion. Heart not enlarged. No heart murmurs. Examination of abdomen shows moderate tenderness on pressure over the gall-bladder and appendix regions. The right rectus muscle is somewhat more tense than the left. Some tenderness on palpation in region of right kidney. Abdominal reflexes present. No abnormalities of genitalia. Cremasteric reflexes present. Sensation on face negative (rough test). No impairment of sensation over upper extremity. Muscular power good; perhaps a little less on right side. Reflexes in extremities present and normal. Rather marked tenderness of calf muscles on left. Babinski equivocal. Muscle sense good. Kernig positive. Brudzynski positive. Coarse tremor of fingers. Marked tenderness in back of neck with some rigidity. Inability to bend head without exquisite pain in neck and back of head. Blood-pressure: 130 systolic; 82 diastolic.

Laboratory Reports.

Blood Examination.

Red blood cells	4,844,800
White blood cells	22,850
Hemoglobin	90 per cent.

Smear, negative for parasites. Wassermann, negative.

Differential count:

Polymorphonuclear neutrophiles	90 per cent.
Polymorphonuclear eosinophiles	1 "
Polymorphonuclear basophiles	1 "
Small mononuclears	2 "
Large mononuclears	5 "
Transitionals	1 "

Cerebrospinal Fluid (First Examination March 7, 1918). Fairly clear fluid; ran out freely, as if under increased pressure. Cell count, 97 small mononuclears. Wassermann, negative in single, double and quadruple quantities. Gold-sol test showed "combined paretic and meningitic curve." Ross-Jones, + + + +. Pandy, + + + +.

A second lumbar puncture (March 7) showed 133 cells. Differential count showed 98 per cent. lymphocytes and 2 per cent. leukocytes. Smear showed no organisms.

Third examination (April 25, 1919). Clear-looking fluid, apparently under increased pressure; 33 cells per c.mm. Ross-Jones, + + + +. Pandy, + + + +, Wassermann, negative in single and double quantities. "Luetic type of curve."

Gastric Analysis.

Free HCl	40 per cent.
Combined acid	25 "
Total acidity	65 "

Otherwise negative.

Stool, normal.

Urine. Reaction acid.

Specific gravity	1012-1014
Sediment	+
Albumin	++
Sugar	0
Phthalein, total 70 per cent. in two hours.	

Microscopically: red blood cells, many; white blood cells, many. "All kinds of casts." Many epithelial cells.

X-ray Reports. *Skull:* Sinuses clear. Sella, normal in size and shape. Head otherwise negative.

Teleroentgenogram. M. L., 6; M. R., 4.5; T., 10; L., 12.

Teeth. Radiographic review reveals slight periapical destruction of the cortical layer of the left upper central.

Special Ophthalmoscopic Examination. Examination of eye-grounds show edges of disks distinct. Physiological cup, deep. Cribriform plate, well marked. Veins not full or tortuous. Arteries normal. Retina, as far as seen, normal.

Psychiatric Examination. Impression, delirium of organic type; no definite symptoms pointing to general paralysis; probably a luetic basis (endarteritis) reinforced by chronic alcoholism.

Dental Examination. Radiographic review justifies extraction of left upper central. Pyorrhea should be treated.

REARRANGEMENT OF DATA IN CASE III.

CASE III (No. 5599).—Male, aged forty-eight years; married.

Complaint. Pain in back of head and neck.

Habits. Alcoholic for many years. Heavy smoker for number of years.

Previous Infections. None.

Respiratory System. Inconstant dry râles throughout both lungs. Lungs in back clear on percussion and auscultation. Tonsils small; not infected.

Circulatory System. Pulse-rate for first week around 90; afterward from 70 to 85. Blood-pressure $\frac{13.0}{8.0}$.

Blood and Hemopoietic System. Red blood cells, 4,844,800; white blood cells, 22,850; hemoglobin, 90 per cent.; polymorphonuclear neutrophiles, 90 per cent.; polymorphonuclear eosinophiles, 1 per cent.; polymorphonuclear basophiles, 1 per cent.; small mononuclears, 2 per cent.; large mononuclears, 5 per cent.; transitionals, 1 per cent.; Wassermann, negative. Smear, negative. No glandular enlargement.

Digestive System. Tongue covered with brownish coat, tremulous; uvula pulled over toward right side. Some pyorrhea; one tooth showing peri-apical rarefaction. Gastric analysis, negative.

Urogenital System. Urine: Specific gravity, 1012–1014; albumin, ++; no sugar; red blood cells, many; white blood cells, many; all kinds of casts; many epithelial cells.

Locomotor System. Negative.

Nervous System. In present illness, pain in head and back of neck. Mind impaired; talk disconnected. No convulsive attacks nor loss of consciousness. Rational periods alternating with periods of delirium, suggesting "uremic poisoning"; suicidal tendencies.

For a few days after onset of illness the patient's face and head were drawn to the right side. Arms stiffened, flexed and drawn across chest. Staggering gait. Marked auditory impairment. No nystagmus; external ocular movements good. Abdominal reflexes normal. Cremasteric reflexes present. No impairment of sensation over upper extremities. Muscular power good; perhaps a little less on left side. Babinski equivocal. Coarse tremor of fingers. Romberg suggestive. Kernig positive. Brudzynski positive. Marked tenderness in back of neck with some rigidity.

Mononucleosis and globulin in cerebrospinal fluid examination with negative Wassermann and "combined parietic and meningitic gold-sol curve."

Metabolic and Endocrine Systems. Thirty-five pounds under weight. Temperature and pulse normal on admission. Second day temperature went up to 104°. Third day normal; remained normal for two weeks. For following ten days slight rise (99° to 99.5°), after which it dropped to normal and remained so until discharge. Very slightly subnormal at times. For first week tachycardia; afterward pulse 70 to 85. Thyroid not enlarged.

DIAGNOSTIC SUMMARY IN CASE III.

1. Acute encephalitis and meningitis.
2. Chronic nephropathy.
3. Oral sepsis.
4. Undernutrition.
5. Chronic alcoholism.
6. Chronic tabagism.

DISCUSSION OF CASE III. In this patient with chronic alcoholism, progressive weakness, loss of weight, delirium and an outspoken nephropathy, it was natural that the case should have been looked upon at first as one of uremic poisoning. The signs of meningeal irritation (rhachialgia; headache; Kernig; Brudzynski) led to lumbar puncture and the findings in the cerebrospinal fluid ruled out meningococcal, tuberculous and luetic meningitis and pointed strongly to epidemic encephalitis with meningeal involvement.

CASE IV.—Male, aged forty-seven years; business man; single. Seen March 13, 1919. (No. 5550.)

Anamnesis (Summary). Always strong. Had scarlet fever in childhood; no sequelae. Never had typhoid fever nor tonsillitis. When thirty-five, had a bubo following urethritis. This was opened and drained; no sequelae. Contracted lues when twenty-nine. Treated at different times. For last five weeks, mercurial inunction every other night and mercurial pills internally. Uses alcohol very moderately. Smokes five or six cigars daily.

Father died of dilated heart in course of diabetes. Mother died of cancer of liver. One brother (living) has "traces of diabetes at

times." Four paternal uncles had diabetes; all lived to fair age; youngest sixty-four. No history of insanity nor of epilepsy in the family.

Present Illness. Had influenza in January, 1919, two months before he was seen. Two days after onset of illness, patient noticed numbness of left arm, left loin and left leg. Sugar was found in the urine about ten days later, but it disappeared after a week of strict diet, and there has been no reappearance up to the last urinary analysis, made on March 1, 1919. When asked to describe his numbness he says he "feels as though he was asleep; has pressure along the finger-nails; has a drawing feeling along the sciatic nerve and outer side of left leg." No thirst. No vertigo. Mind active. He says his eyes are apparently normal. He has walked with a slight limp, but has had no other difficulty in locomotion. No apparent loss of sexual desire or power. No frequency in micturition.

Physical Examination (Summary). Large man, well developed; inclined to corpulence; florid complexion. Present weight 182 pounds. Ideal weight, 150 to 155 pounds. Cranium normal. No tenderness anywhere. Eye slits narrow. No staring; pupils equal and react fairly promptly to light and accommodation. No von Graefe; no exophthalmos; ocular movements normal. Mouth shows a good deal of dentistry; some retraction of gums; some evidence of pyorrhea. Tongue moist; slightly coated. Pharynx red; a little edematous around the uvula. Both tonsils slightly enlarged, showing evidence of former infection. No tophi in ears. Thyroid not palpable. Thorax well formed; expansion good; lungs clear on auscultation and percussion. Heart normal. Pulse 26 to quarter (erect position); full, bounding, poorly sustained, but not collapsing; easily compressed; apparently little if any thickening of the vessel wall. Hepatic dulness at sixth rib extends to the costal margin; spleen not palpable. Abdomen symmetrical, pendulous; wall flabby; some resistance in right hypochondrium, not marked nor painful. No pain on pressure in the right iliac fossa. Crines and hirci normal. No edema of extremities. Reflexes of left arm seem sluggish; right arm active; feeble abdominal reflexes. Knee-jerks on right side seem normal; on the left side sluggish; plantar reflexes on both sides sluggish. Babinski negative. No clonus. Sensibility acute everywhere despite the subjective numbness. No areas of anesthesia. Equilibrium a little unsteady; coördination a little unstable. External hemorrhoids. Some pain over the prostate; rectum normal.

Laboratory Reports.

<i>Blood.</i>		No.	Per cent.
Red blood cells . . .	5,472,000	Polymorphonuclear neutrophiles	190 76.0
White blood cells . . .	10,000	Polymorphonuclear eosinophiles	1 0.4
Hemoglobin	90 per cent.	Polymorphonuclear basophiles	0 0
Blood sugar 210 mg.		Small mononuclears	43 17.2
in 100 c.c.		Large mononuclears	16 6.4
			<hr/>
			250 100.0

Microscopically: Red blood cells and platelets normal. No abnormal cells seen.

Blood Wassermann Reaction:

Antigen A, cholesterinized human heart—negative.

Antigen B, acetone insoluble lipoids—negative.

Antigen C, plain extract beef heart—negative.

Gastric analysis. 75 c.c. recovered; colorless; much residue.

Free HCl 36 acidity per cent.

Combined acidity 53 acidity per cent.

Total acidity 89 acidity per cent.

Occult blood 0

Lactic acid 0

Microscopically 0

Urine analysis. reaction acid.

Specific gravity 1032

Albumin Ft. trace

Sugar 0

Acetone 0

Microscopically: A few hyaline casts. No blood cells. Negative for bile, blood, and indican.

Stool examination. Brown; formed.

Bile +

Occult blood ++

Microscopically Negative

Cerebrospinal fluid

Pressure Normal

Cell count 30

Predominant type of cell Lymphocyte

Globulin +

Wassermann, negative, with three different antigens.

Röntgen-ray Reports: Chest. Heart about normal size. Diffuse dilatation of aorta. The first curve on the right is particularly prominent. Retrocardiac space clear. Lungs and diaphragm show nothing remarkable.

Gastro-intestinal Tract. No fourteen-hour retention. Stomach of cowhorn type, lying rather high and quite far to the right. Pyloric extremity in apposition with the hepatic flexure, but separable from it. No filling defects; no incisura. Hepatic flexure bent rather sharply to the left; not very freely movable. This may be due to obesity. Cecum rather overfull of barium. Transverse colon normal.

Lateral Skull. Sella rather small. Bony outlines not very clear, but the sella is probably negative. The sphenoidal sinus is large; apparently negative. Frontals normal. Tables of skull normal.

Paranasal Sinuses. Slight haziness in the lateral portion of the left antrum. Turbinates seem a little thick.

Teleroentgenogram. M. R. 5.2; M. L., S.S. Heart slightly enlarged; the aorta moderately dilated. There is a good deal of fibrosis along the mediastinal margins, which tends somewhat to obscure the outlines of the aorta.

Neurological Report (Dr. H. M. Thomas). "I was not able to demonstrate any organic lesion. From the patient's history, however, I have very little doubt that he must have some vascular, or, conceivably an inflammatory condition, somewhere in the sensory path. Such a persistent sensory disturbance suggests a lesion near the optic thalamus, although I have seen it associated with softening in the medulla after occlusion of the posterior inferior cerebellar artery."

Oculist's Report (Dr. Hiram Woods). External appearance, muscle movements, pupillary reactions normal. The optic nerve has a central cup rather deeper than usual, but there is no evidence of nerve lesion. There is a concentric contraction for white and red in each eye. The contraction averages about 15° . However, the retina tired quickly. Central vision is normal, with a low manifest hyperopia in the right eye. The patient's glasses are insufficient. The muscle balance test shows a low grade of combined hyperphoria, with a little tendency outward. *All the muscles, except the externi, are deficient in prism power.* The red glass before one eye which in health has no effect, produces a diplopia corresponding with the balance defect.

Rhinologist's Report (Dr. H. C. Davis). 1. Frontal and maxillary sinuses clear on transillumination; nose and nasopharynx free from any discharge that would indicate infection of the paranasal sinuses.

2. Slight obstruction to breathing on right side, due to deviation of septum to that side.

3. Tonsils quite adherent, otherwise do not show any evidence of infection.

4. Uvula quite elongated, but not at all productive of any symptoms.

Psychiatrist's Report (C. Macfie Campbell). Patient showed a degree of placidity that may indicate a slight change in disposition, but there was no euphoria, expansiveness, nor depression. Orientation was correct; memory of the remote past very satisfactory. Good retention of tests; serial subtraction carried out promptly.

No indication of any distorted attitude toward the external world. There is no evidence in the patient's mental status of mental reduction in relation to the organic episode and no evidence of general paresis.

Urologist's Report (Dr. G. Timberlake). Genitalia normal; no discharge from meatus.

Scar from incised bubo on the right side. The urine shows a few shreds that contain small amounts of pus. Anal sphincter normal; rectum seems normal. Prostate normal for age and history. It is smooth, regular in outline, non-adherent, not tender to pressure; the vesicles seem free but palpable. The prostatic secretion shows marked evidence of chronic inflammation, with a preponderance of pus cells. There was an occasional red cell found, probably the

result of pressure. No superficial evidence of lues, notwithstanding the history. Even with the unusual amount of pus cells in the prostatic secretion, there are no referred urinary, sexual, or general symptoms as a result.

Dentist's Report (Dr. Arthur Lankford). General pyorrhea in both upper and lower jaws. Two bicuspid show badly necrosed condition of alveolus; two other teeth are badly undermined. These teeth are quite loose and are no doubt a source of considerable absorption.

REARRANGEMENT OF DATA IN CASE IV.

CASE IV.—(No. 5550.) Male, aged forty-seven years; single; drygoods merchant.

Complaints. Numbness of left arm, left leg and left loin, with tingling. No loss in motion or strength.

Habits. Cigars five to six a day; alcohol in moderation.

Infections. Scarlet fever at three years; urethritis at twenty-five, followed by bubo that was opened and drained; no sequelae. Lues at twenty-nine; treatment. Influenza in January, 1919.

Operations. None.

Traumata. None.

Respiratory System. Lungs negative. Roentgenogram of paranasal sinuses shows slight haziness in lateral portion of the left antrum.

Deviation of septum; elongated septum.

Circulatory System. Pulse, 104. No heart murmurs.

Teleroentgenogram: M. R., 5.1; M. L., 8.8. Aorta moderately widened.

Blood System. Red blood cells, 5,472,000; white blood cells, 10,000; hemoglobin, 90 per cent.; Wassermann, negative; polymorphonuclear neutrophiles, 76 per cent.; eosinophiles, 0.4 per cent.; small mononuclears, 17.2 per cent. Blood sugar, 210 mg.

Digestive System. Free HCl, 36. Total acidity, 89. Occult blood, 0.

Stool contains occult blood. Teeth and gums suspicious. Roentgen rays show sluggish colon; ileal stasis. Four or five teeth to be extracted; pyorrhea to be treated.

Urine and Urogenital System. Urine: Specific gravity, 1032; faint trace of albumin; sugar, negative; a few hyaline casts; red blood cells, 0; white blood cells, 0. Chronic prostatitis.

Locomotor System. Negative.

Nervous System. Left-sided numbness appearing in January, 1919. (two days after onset of "influenza"). Pupils active. Paralysis of external ocular muscles. Reflexes normal on one examination; slight hyporeflexia on left in another. Some contraction of visual fields for white and red; low hyperopia in right eye; external hyperphoria; glasses insufficient; some eyestrain.

Cerebrospinal Fluid. Normal pressure; cells, 30 small mononuclears, globulin, +; Wassermann, negative. Lesion in sensory path (*q. v.*).

Metabolism and Endocrine System. Glycosuria since January, 1919. Much diabetes in family. Hyperglycemia disappearing after diet. Overweight, twenty-five to thirty pounds.

DIAGNOSTIC SUMMARY IN CASE IV.

1. Residue (left paresthesia and hyporeflexia) of slight cerebral lesion in January, 1919. This may have been a slight encephalitis or a slight vascular lesion; the findings in the cerebrospinal fluid point to encephalitis.

2. Slight atherosclerosis, with slight arterial hypertension (blood-pressure: systolic, 163; diastolic, 94).

3. Oral sepsis.

4. Chronic prostatitis.

5. Obesity, thirty to forty pounds overweight.

6. Hyperglycemia with history of glycosuria.

Discussion of Case IV. We were inclined to look upon the cerebral insult (with lesion in the right cerebrum) at first as of vascular origin, but, later on, concluded that the patient had suffered from a mild attack of epidemic encephalitis because of (1) the low grade of atherosclerosis that existed, (2) the paresis of the muscles of the bulbus oculi and (3) the characteristic findings in the cerebrospinal fluid. Whether or not the glycosuria and the hyperglycemia can be brought under the same rubric is difficult to say. It is of interest to note that there is a marked history of diabetes in the patient's family. Though the patient admitted a luetic infection in his twenty-ninth year, lues can scarcely have been responsible for his cerebral lesion, since the Wassermann reaction was quite negative with three different antigens (and with quadruple quantities of fluid) in both the blood and the cerebrospinal fluid.

CASE V.—Female, aged forty-six years; married. Seen March 17, 1919. (No. 5497.) Referred to office for general diagnostic survey by Dr. George H. Brownfield of Fairmont, W. Va.

Complaint. Influenza seven or eight weeks ago; diplopia for six weeks; trouble in seeing; weakness and nervousness; sleeps poorly.

Family History. Practically negative, except that one sister died from tuberculosis.

Personal History. Has had typhoid "three times," last time twenty years ago. Considered tuberculous in youth; subject to colds. Two children living; one died in infancy; no miscarriages. No operations. No traumata.

Present Illness. Influenza seven or eight weeks ago, accompanied by severe pain in the back of the head. Diplopia for six weeks; slight ptosis of eyelids. In bed most of the time since that illness; weak; nervous; unable to read; depressed. Tongue tremulous. Dizziness; timmitus; constipation. Her doctor says her mind is not right. She "wanders" at times. She has always worked very hard.

Physical Examination by Dr. Cross. (Summary). Patient is twenty pounds below calculated ideal weight. There is a little asymmetry of the lower part of the face; the mouth is drawn a little to the right; there is constant twitching of the upper lip and a good deal of twitching of the tongue. The face is mask-like (Fig. 2). Eyes deep set; they seem a little sunken. The eyelids droop a little; there is some injection of the sclerae. Cheeks a little bulging; acra very prominent. Von Graefe negative. Rosenbach slightly positive. Eyes move upward with a rather jerky movement. Convergence is poor, particularly in the left eye. Slight nystagmic movements in the extreme lateral positions. Pupils rather wide, equal; regular; react to light at present. Tonsils scarcely visible. Much dentistry; numerous gold caps and long bridges. Several teeth missing in inferior arch; some gingivitis. Patient has some difficulty in opening the mouth; she thinks the jaw joints are stiff. There is some thyroid enlargement. Retrocervical glands are palpable, but not much enlarged. Breasts hypoplastic. Apex-beat hard to localize. Relative cardiac dullness does not seem to be increased. Heart sounds clear at apex and base. Pulse, 28 to quarter; regular in force and rhythm; vessel wall a trifle thickened. Radial pulsations synchronous. Hands a little unsteady, but no fine tremor. Blood-pressure: 105 systolic, 70 diastolic. Spine negative. Abdomen of enteroptotic type. Liver dullness not increased; edge of spleen not felt. No special tenderness on palpation. Transverse crines. Hirci medium. Knee-jerks present. Abdominal reflexes normal. Arm-jerks equal and active. Grip good and equal in the two hands.

Laboratory Reports.

<i>Blood.</i>			No.	Per cent.
Red blood cells . . .	5,856,000	Polymorphonuclear neutrophiles	207	82.8
White blood cells . . .	10,000	Polymorphonuclear eosinophiles	0	0
Hemoglobin	85 per cent.	Polymorphonuclear basophiles	0	0
Red blood cells and platelets normal.		Small mononuclears	32	12.8
No abnormal cells seen.		Large mononuclears	11	4.4
		Transitionals	0	0
			250	100 0

Wassermann, negative.

Gastric Contents:

Free HCl	0 acidity per cent.
Combined acid	30 acidity per cent.
Total acidity	30 acidity per cent.
Acid deficit	5 acidity per cent.
Microscopically, negative.	

Stool Examination: Negative.

Urine Examination:

Specific gravity, 1010-1016.

Albumin, 0 at first; later a trace.

Sugar, 0

Microscopically, red blood cells, 0; white blood cells a few at times; Hyaline casts at first; (later absent).

Cerebrospinal Fluid (first examination):

About 25 c.c. clear fluid removed.

Pressure, not increased.

Globulin, +; Ross-Jones test, +; Pandy test, +.

Cells, 2 to entire field (lymphocytes).

No film formed in twenty-four hours.

Wassermann reaction, negative.

Second examination (April 4), made in the private ward at the Johns Hopkins Hospital.

Cells, 7 per cm. (lymphocytes).

Ross-Jones, +

Pandy, +.

Wassermann, negative.

Gold-sol test: Atypical paretic curve.

Spinal-fluid culture showed no growth.

Roentgenoscopic Examination of Chest. Heart is small, of pendulous type. Aorta normal. Lungs and diaphragm not remarkable.

Roentgenoscopic Examination of Gastro-intestinal Tract. No fourteen-hour retention; stomach of cowhorn type, lying somewhat downward and to the right. Good peristalsis. Duodenal cap looks normal. No filling defects; no incisura; stomach and duodenum freely movable. Cecum contains a moderate amount of barium. It is easily moved. The transverse colon is prolapsed into the pelvis. The colon seems free of adhesions everywhere along its course. Not much barium in colon.

Roentgenograms of Paranasal Sinuses and Sella. The left frontal sinus is a little hazy, but the ethinoids are clear. The sella turcica is rather small. The clinoid processes tend to approach each other. Bony outline is clear. Sphenoidal sinus negative.

Telereontgenogram: M. R., 4.2. M. L., 6.2. Heart is about normal size. Aorta shows a very slight widening.

Neurological Examination (Dr. H. M. Thomas). Impression: A typical case of encephalitis lethargica.

Gynecological Examination (Dr. Cullen). Outlet normal; no thickening of Bartholin's glands. Cervix small; points downward. Uterus small; freely movable. One small myomatous nodule felt on the posterior wall. Ovaries not felt. No thickening on either side. Rectal examination negative.

Rhinologist's Report (Dr. S. J. Crowe). Impression: Sinuses do not show any evidence of infection. Good breathing through

each side of nose. Tonsils do not show any evidence of chronic infection.

Dental Report (Dr. H. H. Streett). Patient has lost many teeth; including all the posterior teeth that serve for mastication. There are several crowns and bridges, the abutments of which are vital. Superior right second bicuspid is pulpless but shows no periapical rarefaction. No foci of infection are suspected. A slight gingivitis is present in the upper jaw.

Course in Hospital. Admitted March 18, 1919, discharged April 14, 1919. Through period in hospital, temperature showed an elevation (afternoon) of 99° (a few times 100°). Pulse ranged from 90 to 100 and 110. Weight on admission, 117½ pounds; on discharge 123¼ pounds. Steady improvement.

REARRANGEMENT OF DATA IN CASE V.

CASE V.—Female, aged forty-six years; married. (No. 5497.)

Complaints. Influenza seven or eight weeks before; diplopia for six weeks; trouble in seeing. Weakness; nervousness.

Previous Infections. Typhoid fever "three times." Subject to colds.

Operations. None.

Traumata. None.

Respiratory System. Subject to colds. Never had asthma nor hay fever. Thought to be tuberculous in youth. Lungs, nose, throat and sinuses normal.

Cardiovascular System. Radials thickened; low blood-pressure 1 $\frac{0}{7}$ ^{0.5}. Pulse-rate, 112. Heart, negative.

Blood and Hemopoietic System. Red blood cells, 5,856,000; hemoglobin, 85 per cent.; white blood cells, 10,000; polymorphonuclear neutrophils, 82.8 per cent.; polymorphonuclear eosinophiles, 0 per cent.; small mononuclears, 12.8 per cent.; large mononuclears and transitionals, 4.4 per cent. Platelets normal.

Digestive System. Impaired mastication. Good digestion. Appetite poor. Sour stomach. No flatulence. No diarrhea. No jaundice. No gall-stones. Slight hemorrhoids. Achylia gastrica. Constipation.

Genito-urinary System. Menses regular. Three children; no miscarriages. Some leucorrhea. Small myoma on posterior wall of uterus. Slight albuminuria and cylindruria.

Locomotor System. General muscular weakness; jaw-joints "feel stiff."

Nervous System. Asthenia; cephalalgia; dizziness; tinnitus; bilateral ptosis; diplopia; poor convergence; accommodation paralysis; twitching and tremulousness of upper lip and tongue; Parkinsonian mask; tachycardia; paresis of muscles of face, especially on left side; tender masseters; globulin in cerebrospinal fluid; history of change in mood, delirium and insomnia.

Metabolism and Internal Secretions. Twenty pounds under calculated ideal weight; slight struma. Normal trichosis. Slight fever.

DIAGNOSTIC SUMMARY IN CASE V.

1. Acute encephalitis.
2. Achylia gastrica.
3. Myoma uteri.
4. Undernutrition.

Discussion of Case V. In this patient the presence of both general and focal symptoms referable to the nervous system, coming on as an "infectious ophthalmoplegia" and "delirium" after



FIG. 2

FIG. 2.—Case V as seen March 17, 1919. Fever; ophthalmoplegia; left facial paresis; mask-like face; twitching of lips and tongue; nystagmoid movements; tender masseters; asthenia. (Parkinsonian type.)

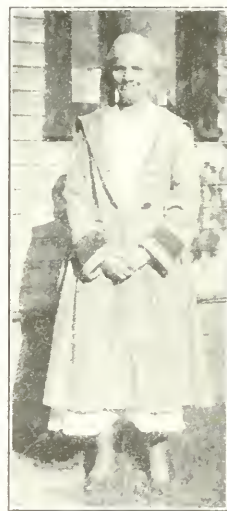


FIG. 3

FIG. 3.—Case V as seen June 1, 1919. At home. Feels entirely well except that vision is still defective. Gain of twenty-one pounds in weight.

influenza, made one think at once of an encephalitis. The pain in the head, the dizziness, the asthenia, the insomnia, the depression and the delirium though pointing to the cerebrum, could scarcely be valued for finer topographical diagnosis. The striking Parkinsonian mask (see Fig. 2) suggested involvement of the nucleus lentiformis (globus pallidus). Otherwise the focal symptoms (ophthalmoplegia externa et interna; twitching of lip and tongue; paresis of left face; tender masseters; tachycardia) pointed to disturbances in the periaqueductal gray matter and the gray matter of the floor of the fourth ventricle (nucleus n. oculomotorii; nucleus

n. trigemini; nucleus n. facialis; nucleus ambiguus; nucleus n. hypoglossi). Les was ruled out by the negative Wassermann reaction in both blood and cerebrospinal fluid. The patient improved rapidly and left the hospital April 14. By June 1 she had gained twenty-one pounds, looked natural (Fig. 3) and felt well, though partial paralysis of accommodation still persisted.

CASE VI.—Male, aged between fifty and sixty years. Seen in consultation, March 25, 1919, with Dr. Sydney R. Miller, of Baltimore, and Dr. Horace N. Mateer, of Wooster, Ohio.

Complaints. Intense lancinating pains in the trunk and in the lower extremities and marked constipation.

Family History. Negative.

Personal History. Patient has enjoyed good health most of his life. He had the ordinary childhood infections, but no severe, nor any infectious, diseases since. No operations. No traumata. He has suffered from some indigestion for years, especially from gaseous eructations after meals. He has used tobacco in moderation. No history of alcoholism. The patient suffered from a nervous breakdown five years ago (anorexia, insomnia, depression), but recovered after treatment in a sanitarium. Two years ago he suffered from a cerebral insult, having been found one morning in a stupor with some paralysis of the right eye, which subsequently cleared up.

Present Illness. About February 19, 1919, he suffered from severe backache, which came on suddenly and without apparent reason. It was taken to be lumbago by his physician. Despite the pain, he went on a visit to relatives in Pennsylvania, and, on arrival, found three cases of influenza in the house. On February 22 he ate rather freely of chicken livers, which he thought were insufficiently cooked. Next morning he awoke with a severe attack of hiccough, which persisted through the day. On the following day, on waking, he had a feeling of pain and constriction around his waistline on both sides. He attributed this to stiffness and pressure caused by a belt. Examination by a physician at that time revealed no definite abnormality. His temperature then was normal. During the following week he improved somewhat and the girdle sensation grew less. On March 1, however, he began to have severe stabbing pains starting in the back in the region of the left kidney and radiating toward the groin. During two or three days following the pains became more severe, especially in the region of the groin, although they were somewhat less severe in the region of the kidney. The pains next extended down the left leg. At the same time he began to have severe pains in the right groin and leg. Still later the pains extended to the leg between the knee and ankle on the right side, where they became maximal. On March 8, about a week after the onset of the pains, the hiccough returned and lasted three or four days without intermission. The hiccough then ceased and has not recurred since.

On March 12 a nurse was secured, and after this time a regular temperature chart was kept. There was a little fever, reaching a maximum of 100.4° on March 20. At this time he suffered also from sudden and severe pain in the right side of the chest, extending into the right arm. Though there was no cough and no increase of the pain on respiratory movements, the physician in charge thought of the possibility of a dry pleurisy and strapped the chest. At about this time, roentgenograms of the kidneys were made, but no shadows of stone could be found. At the time the hiccough subsided the patient states that he was very drowsy for a period of four or five days, much drowsier the nurse thought than the sedatives given for the relief of pain could account for. The nurse described the patient's behavior as "much like that of a man who is coming out of an attack of drunkenness."

The pains in the right lower extremity have persisted from the onset. They have been more severe at night and have greatly disturbed his sleep. The patient describes the pains as being somewhat intermittent. He states that they are rather superficial, "as though they were in the skin rather than in the muscles or bones." The nurse thought that when she first saw him there was distinct unsteadiness in his gait and a little dragging of the right leg. There has been no history of eye-muscle disturbance.

Physical Examination (Dr. Barker and Dr. S. R. Miller). March 25, 1919. Summary: Patient lies quietly in bed. Does not look ill. External ocular movements normal; no diplopia; right pupil somewhat sluggish; double arcus senilis. Teeth look suspicious. Lungs clear. Heart normal. Low blood-pressure. Abdomen negative. Genitalia negative. No objective disturbances of sensation on rough testing. Muscular strength everywhere good. Knee-jerks somewhat overactive. No actual clonus. Babinski negative. Abdominal reflexes normal. Patient walks with rather a broad base and is somewhat unsteady. Romberg suggestive. Heel-knee test and finger-nose test done well. Calculation good. No disturbance of speech. Lumbar puncture had been done two days earlier and patient felt much better afterward.

Impression. Encephalomyelitis with meningitis and spinal radiculitis.

Laboratory Tests. Blood Wassermann done on March 24, 1919, was negative, with three different antigens. Urine, March 24, negative except for a faint trace of albumin and a good many white blood corpuscles. Cerebrospinal fluid, March 24: clear, colorless, pressure much increased, cell count 48, all small mononuclears, globulin 3 plus, Wassermann reaction negative, with three antigens in quadruple quantity. Second examination of spinal fluid, March 31, showed 14 small mononuclear cells and globulin 4 plus; Wassermann negative. Third examination, April 5: pressure increased, but less than before; 14 cells, globulin 4 plus; Wassermann negative.

Blood examination, March 30, 1919: Red blood cells 4,800,000; white blood cells, 9000; hemoglobin, 85 to 90 per cent. Smear shows nothing abnormal.

Urine examination, March 30: Negative except for faint trace of albumin and many white blood corpuscles; no red blood cells; no casts.

Stool examination, March 30: negative.

Urogenital Consultation (Dr. G. Timberlake), March 31, 1919. Urogenital tract practically negative. Rectum negative.

Neurological Consultation (Dr. H. M. Thomas), April 1, 1919. "The history is remarkable on account of the intense shooting root pains, which give a sharp segmental localization. The patient's description of their running to a certain place on the abdomen and then stopping abruptly is very striking, as is also his description of the gradual increase of the painful area involving segment after segment. A meningeal process must have involved the posterior roots in a descending order. It is also remarkable that the process seems to have been almost exclusively an irritative one and to have left no symptoms of destruction either of the roots themselves or of the substance of the spinal cord, unless the somewhat irregular Oppenheim on the right side be considered as such.

Dictated Note. Patient looks rather listless. Face not mask-like. Can read well with glasses. Eye-grounds negative. Pupils dilated, right more than left. Pupils react directly and consensually to light. Reaction is more active in the left pupil than in the right. Eye movements normal. Masseters normal, not tender. Hearing normal. Facial muscles normal. Jaw-jerks active. Possibly a little weakness of the abdominal muscles. Abdominal reflexes not obtained. Kernig negative. Knee-jerks active and equal. No clonus. Oppenheim positive on the right, negative on the left. No objective disturbances of sensation. When the legs are flexed at the hips the adductor muscles seem to go into a temporary clonus. No pain along the course of the large nerve trunks at present. Station with the feet together now quite steady.

Impression. Epidemic encephalitis, with special involvement of the meninges and spinal nerve roots."

Course. The patient remained in a nursing home for about two weeks and improved rapidly, apparently being much benefited by lumbar punctures and by rest. Dr. Mateer wrote on May 15 that the patient, after returning home had developed no untoward symptoms and was slowly regaining his strength.

Discussion of Case VI. The case was a puzzling one at first, as far as diagnosis was concerned. Except for the acuteness of the onset and the absence of a luetic history the segmental pains suggested the lancinating pains of tabes; and as the pains were worse at night, there had been some unsteadiness of gait and the lumbar puncture showed an increased cell count of small mononuclears and a positive

globulin, a paraluetic process was seriously thought of and preparations were made to give antiluetic therapy. However, the Wassermann test of the blood turned out to be negative, as did also the Wassermann reaction in the cerebrospinal fluid. On reviewing the history, the mode of onset with backache, hiccough and drowsiness, followed by a little fever, acute encephalomyelitis came to mind as a probability-diagnosis, especially as other cases of the disease were being seen at about this time. It was remarkable, however, that there was no paralysis of the eye muscles, with the exception of a sluggish right pupil, and no involvement of the other cerebral nerves. The hiccough suggested an irritation in the region of the phrenic in the cervical enlargement of the spinal cord. The weakness of the abdominal muscles and the temporary disturbance of coördination suggested a possible involvement of the cerebellum or of its connections.

A final consideration of the case leads us to think that there must have been a widespread involvement of the central nervous system and its coverings in this instance, with predominant involvement of the spinal meninges and of the spinal nerve roots. The drowsiness points probably to the telencephalon, the sluggish right pupil to the mesencephalon, the weakness of the abdominal muscles and the incoördination to the cerebellum and its peduncles, the hiccough to the nucleus of origin of the phrenic in the cervical enlargement of the spinal cord and the severe segmental pains to the meninges and to the posterior roots of the spinal nerves. We therefore made a final diagnosis of meningo-radiculo-myelo-encephalitis in this case. The recovery of the patient supports the view.

CASE VII.—Colored female, aged thirty-three years; married.
Complaint. "Misery in eyes and head."

Anamnesis: Family History. Mother died at forty of heart trouble.

Personal History. Never seriously ill; none of the exanthemata. Occasional headache. Did not have influenza and has had no colds recently. Does not use stimulants. Eight children; five living; no miscarriages. Best weight, 105 pounds, one year ago. Weight on admission 90 pounds (stripped).

Present Illness. One week ago, while working, the patient suddenly felt "dizzy." Then she "saw double." The dizziness passed off; but she has continued to see double. Since then she has had frequent headaches, which are relieved by lying down. Three days after the onset of this illness she noticed a sensation of "grit in her eyes," which has persisted. She has felt weaker than usual and her appetite is poor; otherwise she feels normal, except for her eyes and head. She has not gone to bed in the day-time except to get relief from the headache. She has felt drowsy but the drowsiness has not prevented her from working. She felt sleepy while talking, but only

once fell asleep during conversation. She has had some difficulty in swallowing, and notices that food sticks in her right cheek. Temperature, 99°; pulse-rate 100. Respirations 20. Blood-pressure: 126 systolic, 88 diastolic.

Physical Examinations (Dr. Bloomfield, Dr. Harrop and Dr. Hermann) (*Summary*). Eighth day of disease. Patient has distinctly mask-like expression. No disturbance of smell nor of vision. Complains of diplopia, the two images being very close together. No obvious strabismus. There is a distinct sluggishness and uncertainty in the movements of all the eye muscles. The bulbs can be moved pretty well, however, medialward and downward. There is very little upward movement and slow, incomplete lateral movement. Distinct incoördination of bulbs on looking to the side. Pupils are equal. Distinct weakness of the motor branch of the fifth nerve. Slight facial asymmetry and drooping of the right eyelid. Facial movements seem a little weaker on the left side than on the right. Hearing is normal. No sign of bulbar involvement. No stiffness of neck.

Kernig negative. Strength of arms and legs good and equal. Reflexes normal except right knee-kick is a little more active than the left. There is sweating about the mouth and nose, largely confined to the right side. Eye-grounds normal. Impression: lethargic encephalitis.

Laboratory Reports.

Blood.	No.		Per cent.
Red blood cells . . .	6,326,000	Polymorphonuclear neutrophiles	76
White blood cells . . .	9,120	Polymorphonuclear eosinophiles	1
Hemoglobin	77 per cent.	Polymorphonuclear basophiles	1
Blood culture. No growth.		Small mononuclears	13
Wassermann, negative.		Large mononuclears	9
		Transitionals	0

Throat Culture:

Nasopharynx, negative for influenza bacillus.

Cerebrospinal Fluid:

Bloody.

Pressure, not increased.

Culture showed *Staphylococcus albus* (probably a contamination).

Urine Analysis. Reaction acid:

Specific gravity, 1022-1024.

Sugar, 0.

Albumin, 0 (faint trace once).

Microscopically epithelial cells and white blood cells. No acetone. No guaiac.

Röntgen-ray Reports. Sinuses; negative.

Specialists' Reports. Neurologist. Pupils regular and equal. React fairly to light and sluggishly to accommodation. Unable to read for

a week previous to examination. Visual fields show concentric contraction (rough determination). Extra-ocular movements limited laterally both to left and right. Normal in other directions, but slow and jerky. No spontaneous internal strabismus, but medial rectus lags on right side when looking far to left.

Nystagmus when looking to the right. Marked lacrimation. No exophthalmos. Slight ptosis of right eyelid. Muscle strength of lids equal, but poor. Ophthalmoscopic examination negative. Jaw muscles rather weak on both sides. Patient wrinkles brow, whistles, etc., quite well. There is a slight flattening of the nasolabial fold on the right. Gait is slow, but otherwise normal.

Electrical Tests. Branches of the facial nerve respond normally to faradic stimulation on the right side. On the left side all branches respond, but require a stronger current. The orbicularis oris reacts to direct stimulation, much better on the right than on the left. On both sides the orbicularis oris contracts, with a quick sharp contraction to galvanic stimulation.

Neurologist's Report (Dr. H. M. Thomas). Patient has a peculiar set facies. There is still marked weakness of upward and downward movements of eyelids and eyeballs. Accommodation probably paralyzed. Masseters still sensitive. Otherwise conditions are normal (April 2, 1919).

REARRANGEMENT OF DATA IN CASE VII.

CASE VII.—Female, aged thirty-three years; married; eight children, five living. No miscarriages.

Complaints. "Misery in eyes and head."

Previous Infections. None.

Operations. None.

Respiratory System. Negative.

Circulatory System. Negative.

Blood System. Red blood cells, 6,328,000; white blood cells, 9120; hemoglobin, 77 per cent.; polymorphonuclear neutrophiles, 75 per cent.; polymorphonuclear eosinophiles, 1 per cent.; polymorphonuclear basophiles, 0 per cent.; small mononuclears, 16 per cent.; large mononuclears 7 per cent.; transitionals, 0.5 per cent. (Second examination, April 25): Red blood cells, 6,512,000; white blood cells, 9820; hemoglobin, 75 per cent. Differential Count: neutrophiles, 76 per cent.; polymorphonuclear eosinophiles, 1 per cent.; polymorphonuclear basophiles, 1 per cent.; small mononuclears, 13 per cent.; large mononuclears, 9 per cent.; transitionals, 0. Blood culture negative.

Digestive System. Negative.

Nervous System. Pupils regular and equal; react fairly to light but sluggishly to accommodation. Accommodation paralysis. Diplopia. Visual fields show concentric contraction. Limitation

of extra-ocular movements to left and right. No spontaneous internal strabismus, but right eye fails to move adequately when looking far to the left: Nystagmus to right. Marked lacrimation. Slight ptosis of right eyelid. Ophthalmoscopic examination negative.

Diagnosis. Encephalitis non-purulenta epidemica.

Discussion of Case VII. The onset in this case was entirely typical with headache, dizziness, diplopia, burning or gritty sensation in the eyes, asthenia and drowsiness. The ophthalmoplegia pointed to the midbrain (nucleus n. oculomotorii), the facial mask to the globus pallidus, the lethargy to the cerebrum, the facial and trigeminal paresis to the pons, and the headache to the meninges. In colored people, we are always on the lookout for tuberculous and for luetic meningitis, but the laboratory findings ruled both out. The patient made a good recovery.

CASE VIII.—Female, aged fifty-two years. Referred for diagnostic study, April 14, 1919, by Dr. J. W. Preston, of Roanoke, Va.

Complaints. Loss of weight, depression, nervousness, and a little fever every day.

Anamnesis:

Family History. Negative.

Personal History. Never very strong; had a severe fall on her abdomen at sixteen; suffered from peritonitis in 1892 and in 1900 had her appendix removed, one ovary removed and uterus suspended. She has had amenorrhea for the past eighteen years. The patient says that she has always been energetic and very interested in anything in which she is engaged. She has had domestic worries for some years, and during the past two years has gradually lost weight and has suffered from indigestion, insomnia, depression and anxiety; during this time, she once consulted a psychiatrist, who made a diagnosis of "psychasthenia with unreality complex."

Present Illness. One month ago, while in Florida, she began "to see double;" this diplopia was accompanied by nausea. She went to bed for two or three weeks and every afternoon her temperature rose to 100°. During this time she was very drowsy; she felt sure she "must be being doped," especially during one week. Since then she has been unusually weak, has suffered from dyspnea on exertion, has had tinnitus in the left ear and has been a little dizzy.

Physical Examination (Dr. Sydney R. Miller and Dr. Barker, April 14, 1919). Patient is about ten pounds under ideal weight; looks pale; external ocular movements seem normal; no diplopia at present; left pupil a little larger than the right, but regular in outline; pupils react to light and accommodation, somewhat sluggishly. Moderate arcus senilis. Nasal obstruction on the left. Much dentistry; long history of pyorrhea; many suspicious teeth.

Tongue is protruded in the middle line; tongue very tremulous. Pharynx negative; tonsils small. No general glandular enlargement. Thyroid not enlarged. Pulse 21 to the quarter, regular; radials not thickened; blood-pressure: systolic, 114; diastolic, 70. Lungs negative. Heart negative except for slight tachycardia and a little accentuation of the pulmonic second sound. Old appendix scar in the abdomen; slight abdominal tenderness on pressure; liver and spleen not enlarged. Deep reflexes active. No edema.

Laboratory Reports.

<i>Blood.</i>		No.	Per cent.
Red blood cells	5,408,000	Polymorphonuclear neutrophiles	176 70.4
Hemoglobin	97 per cent.	Polymorphonuclear eosinophiles	1 0.4
White blood cells	17,600	Polymorphonuclear basophiles	1 0.4
		Small mononuclears	57 22.8
		Large mononuclears and Transitionals	15 6.0
			<hr/> 250 100.0 <hr/>

Blood culture: Negative.

Microscopically: Red blood cells and platelets normal. No abnormal cells seen.

Blood-Wassermann Reactions: April 16, 1919.

Antigen A: Cholesterinized human heart, negative.

Antigen B: Acetone insoluble lipoids, negative.

Antigen C: Plain extract of beef heart, negative.

Gastric Analysis:

25 c.c. recovered; normal color.

Free HCl	32 acidity per cent.
Combined acid	13 acidity per cent.
Total acidity	45 acidity per cent.
Occult blood	0
Lactic acid	0
Microscopically, negative.	

Stool Examination:

Bile, +
Occult blood, 0
Microscopically, negative.
Brown, formed.

Urine Analysis:

	Night acid.	Day acid.
Specific gravity	1014	1004
Albumin	0	0
Sugar	0	0
Acetone	0	0
Microscopically few white blood cells.		
Indican	0	0
Bile	0	0

Roentgen-ray Reports. Chest: Negative.

Gastro-intestinal Tract. Negative except for cecal stasis and some ileal retention in the six-hour plate.

Paranasal Sinuses. Negative.

Sella Turcica. Negative.

Psychiatric Report (Dr. Adolf Meyer). "The examination of this patient shows that she is under a very great strain, dependent altogether on an adjustment of a problem which she has not personal control of. The reaction became intensified during the wedding of her daughter last August and the patient has since then, in February, gone through a condition which suggests an abortive encephalitis, but which was evidently closely connected with exacerbations of the continual dread of the recurrence of the matters which upset her so. There is no special difficulty of concentration or memory; no fundamental and unshakable mood disturbance, and I feel convinced that the removal of the cause for uneasiness through radical treatment of the one more directly at the bottom of the condition will yield a satisfactory and lasting result. I should urge a rest period away from the existing cause."

Neurological Examination (Dr. Henry M. Thomas). Patient's voice is normal. Pulse rather rapid; beats at 96. Blood-pressure, 110. Ophthalmological examination. Right optic nerve: Edges are all distinct; physiological cup is not well marked; veins normal in size; there is some pulsation in the central vein; arteries a little tortuous; no marked sclerosis; retina, as far as seen, normal. Left optic nerve: Temporal edge distinct; nasal edge can be made out; is not so clearly seen; upper border is somewhat obscured; veins are of normal size; arterial walls glistening; these are rather small and have a tendency to obliterate the veins.

Pupils equal; react to light directly and consensually and contract during accommodation.

Movements of the eyeballs excellent to the right, left, up and down. Convergence normal.

Muscles of mastication act well and equally. They are not particularly sensitive to pressure.

Jaw-jerk present, not exaggerated.

Sensation on face normal.

Facial muscles act well and symmetrically. Patient has no difficulty in puckering lips and in whistling.

Hearing is acute in both ears.

Soft palate acts equally on the two sides, but not very actively. Tongue is protruded straight; it is slightly tremulous.

Movements of the hands are coördinate. There is no noticeable tremor. Muscular strength is what would be expected.

Biceps and triceps reflexes present and equal. No trouble in recognizing objects placed in hand.

Station with feet together and eyes closed is quite steady.

Abdominal muscles act strongly. Abdominal reflexes are not obtained.

Knee-heel test is done very well on both sides.

Muscular strength of legs is excellent.

Knee-jerks present, equal, not exaggerated. Ankle-jerks present, equal, not exaggerated.

Plantar stimulation gives plantar flexion.

Impression: "The patient's history interests me. She seems to have had a very mild attack of lethargic encephalitis. I could, however, find no present evidence of any permanent defect. For the rest, she is in a highly neurotic, depressed condition, due, I think, to her family worries. She certainly needs an upbuilding treatment."

Dental Report. Roentgenographic review of the mouth shows No. 9 the left superior central, No. 10 the left superior lateral, No. 11 the left superior canine to be periapically infected; they are pulpless teeth, well filled, but they should be extracted and the sockets should be curetted. Replacement is possible on present denture. Bridge "A" should be sectioned between the left inferior first molar No. 19 and the left inferior second bicuspid No. 20. The left inferior second molar No. 18, No. 23 the left inferior lateral, No. 24 and No. 25 the inferior centrals, No. 26 the right inferior lateral, No. 28 and No. 29 the right inferior bicuspids, are periapically and gingivally involved; they should be extracted and the sockets should be curetted. Replacement is possible by removable denture. These teeth could be active factors for focal infection. Those teeth allowed to remain are very important for the retention of the denture and for occlusion.

Gynecological Report (Dr. T. S. Cullen). "I do not find any marked tenderness at any point in the abdomen, though she says there is a slight feeling of soreness. The outlet is moderately relaxed; the cervix is back; the body of the uterus is small but in perfect position; it has probably been attached to the anterior abdominal wall. On the left side, and apparently attached to the uterus, is a globular mass about 3 cm. in diameter, which would correspond to a normal ovary or to one that was just a little enlarged. I can find nothing in the pelvis that will in any way account for the slight fever, and there is nothing in the vagina or pelvis to warrant my suggesting any operative procedure."

Ophthalmological Report (Dr. Hiram Woods). "The patient told me about the moderate "elevation of temperature" dating back some time, and of the presence of "pus in the urine," also of occasional "attacks of burning in the eyes," and, about two months ago, the occurrence of diplopia. This gradually wore off in the course of a month and was accompanied, in its later stage, and followed, by stupor; she says that "she slept for days like one dead." Shortly after getting about her glasses were changed, the last ones being twice the strength of the old. Now the new glasses are uncomfortable and the weaker ones are more satisfactory.

Examination revealed normal media and fundus; pupils of equal size with normal reaction—possibly a little sluggish—but this is not of much importance save as fitting in with my theory that she

has had an encephalitis. She has no manifest refraction error and only a very little hyperopia. It does not need correction for distant vision. Omitting the old "burning" and the moderate fever, both of which may be due to some focal infection, the recent history of diplopia, the temporary decrease in accommodation and the stupor correspond quite closely with what I have seen in some cases of encephalitis recently. The double vision is due to insufficiency of the lateral recti, and, I think, especially of the left. I lent her glasses from my trial case, correcting her presbyopia."

Nose and Throat Examination (Dr. H. C. Davis). Examination negative except for deviated septum and oral sepsis.

REARRANGEMENT OF THE DATA IN CASE VIII.

Chief Complaints. Loss in weight; nervousness; fever daily.

Infections. "Peritonitis," 1892.

Operations. Traumatata. Severe fall on abdomen at sixteen; one ovary and part of other removed in 1900; also appendix removed and uterus suspended; 1895 D. and C.

Respiratory System. Left nasal obstruction; lungs, 0. Deviated septum. Roentgen rays: paranasals 0. Lungs: Old tuberculosis in right upper; no signs of activity now.

Circulatory System. Dyspnea and palpitation at times; pulse, 84; heart, negative; blood-pressure, $\frac{114}{70}$.

Blood and Hematopoietic System. Red blood cells, 5,408,000; hemoglobin, 97; white blood cells, 17,600; Wassermann, 0; polymorphonuclear neutrophiles, 70.4; polymorphonuclear eosinophiles, 0.4; small mononuclears, 22.8.

Digestive System. Free HCl, 32; total acidity, 45; occult blood, 0; stool, 0. Pyorrhea; bowels regular; two years ago indigestion began; heavy feeling; suspicious teeth; slight diffuse abdominal tenderness. Roentgen rays: Sluggish gastro-intestinal tract.

Dental. Ten teeth to extract. Pyorrhea.

Urine and Urogenital System. Urine: specific gravity, 1014, 1004; alb., 0; sugar, 0; cyl., 0; white blood cells, few; red blood cells, 0.

Menopause, seventeen years ago; pyuria once; nocturia, 2 to 3.

Gynecologist: Globular mass on left; probably ovary attached to uterus.

Nervous System and Sense Organs. Trouble in left Eustachian tube for one year; family worries for years; some time ago consulted psychiatrist; evidently "psychasthenic state, with unreality complex"; few weeks ago, double vision, very drowsy, afternoon fever; in bed two to three weeks; left tinnitus for three months; left hippus; slight anisocoria; active pupils; moderate arcus; tremulous tongue; abdominal reflexes absent.

Ophthalmologist: Slight hyperopia and presbyopia; evidently has had encephalitis; ordered reading glasses.

Psychiatrist: Under great strain; evidently recent abortive encephalitis.

Neurologist: Nervous condition; evidently has had mild lethargic encephalitis.

Metabolism and Endocrine System. Fever since September, 1918; undernutrition 8 to 10 pounds; tremor; roentgenogram of sella negative.

Course. The patient entered a nursing home, where she had the ten infected teeth extracted and the pyorrhea treated, and where she received general upbuilding treatment and psychotherapy. After the extraction there was for a time a rather marked anemia. The blood examination on May 16, 1919, showed:

Red blood cells	3,600,000
Hemoglobin	70.0 per cent.
White blood cells	3000
Polymorphonuclear neutrophiles	72.4 per cent.
Polymorphonuclear eosinophiles	1.2 per cent.
Small mononuclears	18.0
Large mononuclears and transitionals	8.4

There was slight anisocytosis; the platelets were reduced.

Though the patient was very psychasthenic during her stay, she improved steadily and has gone to a cool place to spend the summer.

Diagnosis. 1. Convalescence from mild epidemic encephalitis.

2. Oral sepsis: ten teeth to extract; pyorrhea to treat.

3. Psychasthenic state.

4. Refraction error.

5. Moderate undernutrition.

Discussion of Case VIII.—The diplopia, the abducens paresis, the anisocoria, the stupor and the low grade of fever, followed by asthenia and by an exacerbation of a long-standing psychasthenic state led us to the diagnosis of a mild encephalitis, especially as the symptoms appeared at a time when encephalitis was epidemic. Unfortunately, owing to the protest of the patient, no examination of the cerebrospinal fluid was made in this case. The oral sepsis, the psychasthenic state, the undernutrition, and the secondary anemia were more important as therapeutic indications than the mild encephalitis.

(To be concluded)

CONCERNING SPINAL CORD TUMORS AND THEIR SURGICAL TREATMENT.¹

BY CHARLES A. ELSBERG, M.D.,
NEW YORK.

FREQUENCY AND LEVEL. Spinal tumors occur most often outside of the cord. They originate either from the cord itself, from the spinal membrane or from the soft tissues surrounding the dura. Of 67 spinal tumors operated upon by the writer, 49, or almost three-fourths, were extramedullary, and 18, or one-fourth, were intramedullary. In 42, or 62 per cent., of the cases the new growth occurred inside of the dura mater.

TABLE I.

Level.	Extramedullary.	Extradural.	Intramedullary.	Totals.
Cervical	1	2	..	2
	2	1
	3	1
	4	1
	5	2	..	2
	6	3	..	2
	7	1	1	5
	8	1
Dorsal	1	1
	2	5	1	1
	3	..	2	1
	4
	5	1	1	..
	6	1
	7	1
	8
	9	3	1	3
	10	3	..	2
	11	3	1	..
Lumbar	12	3
	1	2
	2
	3
	4
Conus and cauda	5
	..	11

Totals	42	7	18	67

Spinal tumors are met with most often in the cervical and dorsal regions and between the roots of the cauda equina. Thus of the 67 cases of our series, in 27 the tumor lay somewhere between the

¹ From the Surgical Services of Mount Sinai Hospital and the Neurological Institute, New York. Tumors of the spinal cord, spinal membranes and those of the soft tissues which have grown into the spinal canal and have caused compression of the spinal cord are here considered. Primary and secondary malignant growths of the vertebrae and ribs are not included.

fifth cervical and the third dorsal and in 21 between the ninth dorsal and first lumbar segments; in 11 between the lower end of the spinal cord and the roots of the cauda equina. The extramedullary growths occurred with about equal frequency at the cervicodorsal and dorsilumbar levels, while intramedullary tumors were met with twice as often in the cervicodorsal as in the lower levels of the cord.

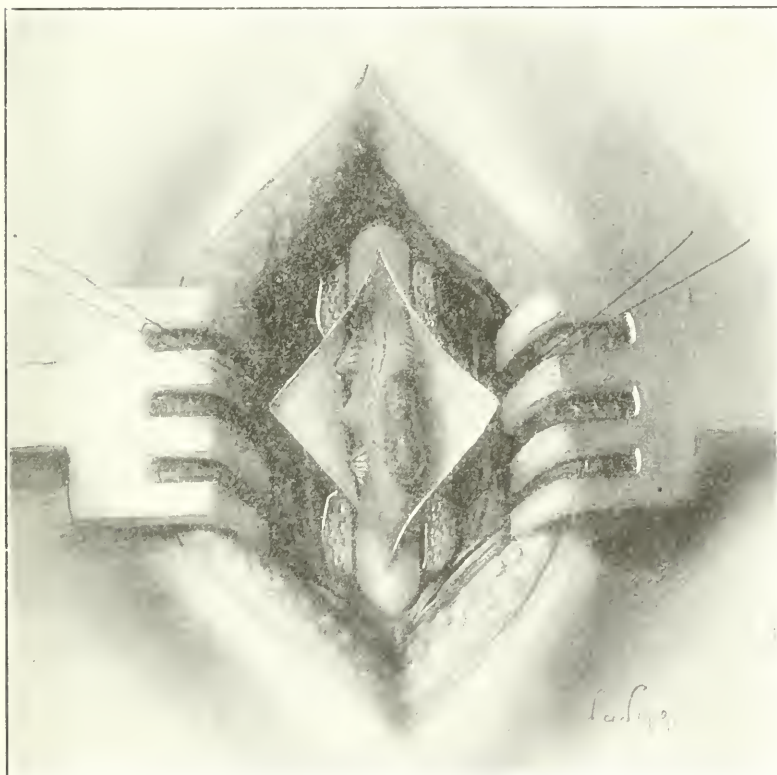


FIG. 1.—Spinal cord tumor (fibroma) on the posterior surface of the cord near the median line.

THE RELATIONS OF THE TUMOR TO THE SPINAL CORD AND TO ITS SURROUNDINGS. Tumors are most frequently met with on the posterior aspect of the spinal cord. They often lie in or near the median line over the origins of the posterior spinal nerve roots; they may develop more to one side of the cord behind the roots of that side (Figs. 1, 2 and 3).

As the dentate ligament marks the boundary between the anterior and posterior halves of the cord, any tumor that develops behind the dentate ligament must be considered as lying on the dorsal aspect of the cord. Some growths develop in front of the posterior roots,

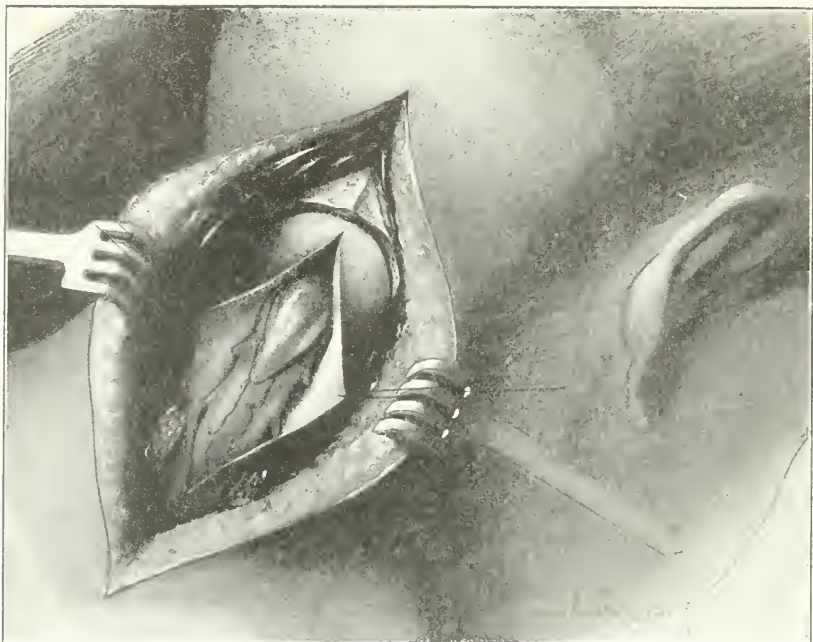


FIG. 2.—Mrs. G. Intradural dermoid cyst lying on the posterior surface of the upper cervical cord and projecting into the posterior cranial fossa.

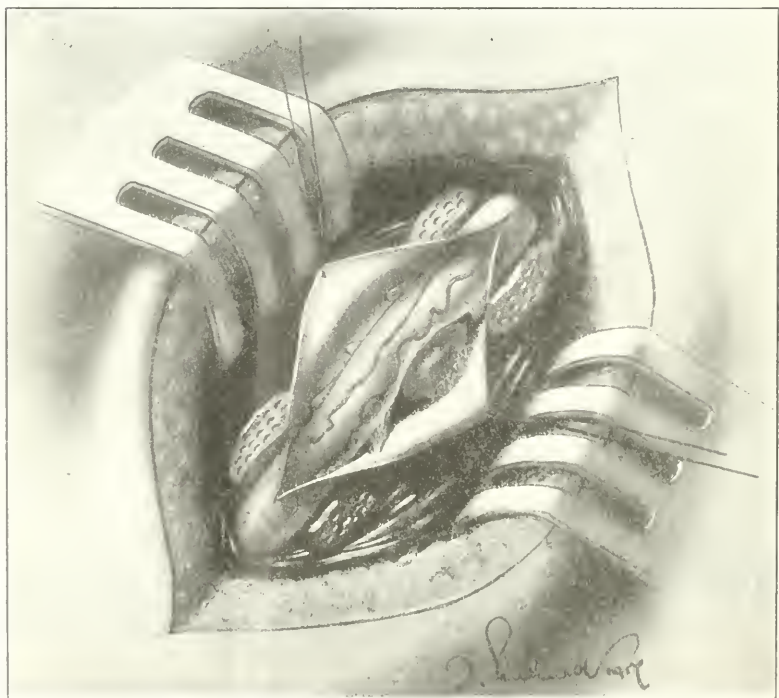


FIG. 3.—F. G. Extramedullary tumor lying behind a posterior spinal root on the

but behind the dentate ligament, and these stretch the posterior roots as they enlarge (Fig. 4). These growths are most liable to cause severe root pains from the beginning of the symptoms. In a patient with a suspected spinal cord tumor, unilateral root pains, followed by cord symptoms, for a long time referable to that side of the cord, justify the probable diagnosis of a cord tumor which has developed under one or more posterior spinal roots.



FIG. 4.—Extramedullary tumor lying in front of a posterior spinal root.

If these patients are seen in a relatively early stage of their spinal cord symptoms a typical Brown-Séquard syndrome may be observed. While an indication of a Brown-Séquard picture—more motor disturbances on the same side and more marked loss of sensation on the opposite side—is seen in all but the advanced stages of the disease a typical Brown-Séquard syndrome is most liable to occur in these extramedullary growths which develop posterolaterally between the dentate ligament and the posterior spinal nerve roots. These tumors develop either from the pia arachnoid covering of a posterior spinal root or from the general pia or arachnoid. Un-

doubtedly they often increase in size very slowly, so that many months and perhaps years may elapse before they have grown sufficiently to compress the spinal cord.

The dentate ligament probably offers considerable resistance to the forward enlargement of the new growth, and the nerve roots may be so tightly stretched over the latter that they have to be divided by the surgeon before the tumor can be removed. These lateral growths are liable to push the spinal cord markedly to the opposite side of the spinal canal.

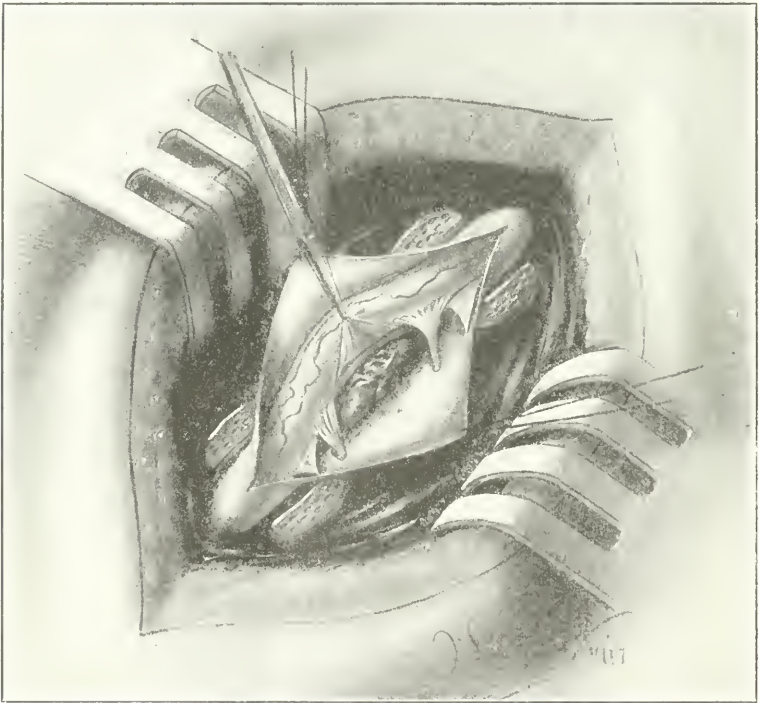


FIG. 5.—Extramedullary tumor lying on the anterolateral surface of the cord in front of a slip of the dentate ligament.

Of the 31 extramedullary (intradural) tumors of our series above the level of the cauda equina, 24, or 77 per cent., lay either on the posterior surface of the cord or posterolaterally, and 14 of the 18 cases of intramedullary tumor seemed to occupy more especially the posterior parts of the spinal cord.

In 7 patients with extramedullary tumors (33 per cent.) the growth was found either anterior or anterolateral to the cord. Here again the tumors may develop either in front of the spinal cord and the anterior spinal roots or anterolaterally between the anterior roots and the anterior surface of the dentate ligament. When these

growths are exposed by the surgeon they are usually found to be covered, on their posterior surface, by the dentate ligament or one of its slips. Usually, one of the attachments of the ligament to the inner surface of the dura has to be divided and the ligament has to be retracted before the tumor can be sufficiently exposed for its removal (Figs. 5 and 6).

These anterolateral growths only rarely begin with root pains; their course is often a painless one and it is frequently difficult to differentiate them from intramedullary growths.

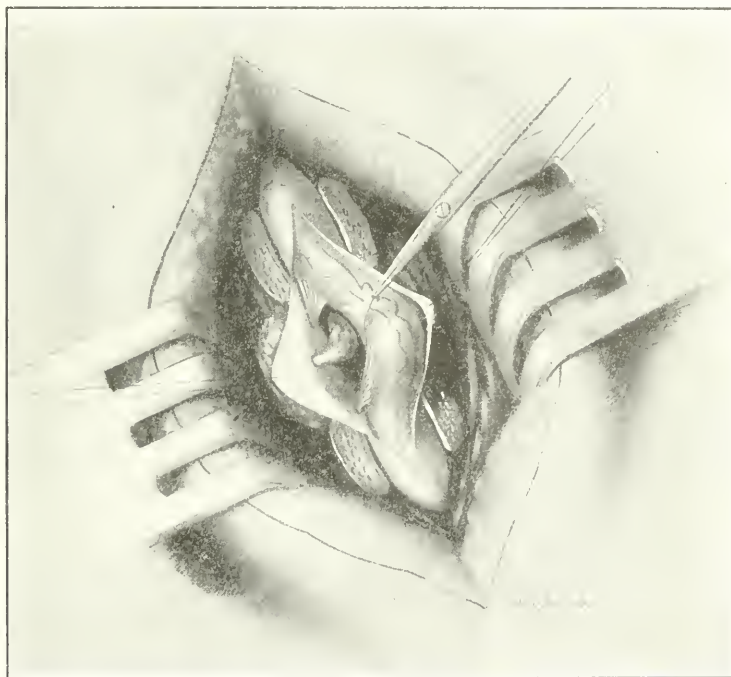


FIG. 6.—Exposure of a tumor lying in front of the spinal cord by traction on a slip of the dentate ligament. (Note that the growth is an extension of an extradural tumor.)

It is often impossible to decide upon the part from which an extramedullary tumor has originated. If a growth is attached only to the inner surface of the dura it has very probably originated from that membrane. Likewise, if the tumor is not adherent to the dura and does not involve any nerve root it must be derived either from the arachnoid or pia mater; in this connection it is well to remember that tumors which arise from the pia are much more closely adherent to the cord than arachnoid new growths.

If the tumor is found to be adherent to several of these structures its origin cannot be determined with certainty. It is sometimes very

difficult to differentiate between a subpial or septal newgrowth and a true intramedullary one. These septal and subpial tumors may be surrounded on all sides by cord tissue, and for their removal an incision into the cord may be required. It may very well be possible that some of the growths we have described as intramedullary were really examples of septal or subpial tumors which had grown into and become buried, as it were, in the tissue of the cord.

INJURY TO THE CORD BY A TUMOR IN ITS PROXIMITY. Every expanding lesion within the spinal canal will, sooner or later, exert pressure upon the spinal cord, but the amount of compression is not directly proportionate to the size of the growth or its duration. Large tumors are more liable to be of softer consistency than small ones, and it is the small, hard tumors that cause, in many instances, early severe damage to the cord structure.

It is often impossible to determine from the appearance of the cord at the time of the operation how great the actual damage has been. Nor can deductions be drawn from the symptoms and signs which the patient presents. If a flaccid paraplegia with loss of all reflexes is present, or if such a condition has existed for a considerable period, it is very probable that the cord lesion is an irremediable one. This does not mean, of course, that there may not be some return of power and of reflexes after the removal of the tumor, but the chances for an amount of improvement that will be functionally valuable for the patient are very slight. The majority of these patients with advanced signs of cord compression, however, have a spastic paralysis which is either a paraplegia in flexion or in extension. Some of the patients, even after years of spastic paraplegia, begin to improve after the removal of the tumor and may recover a very satisfactory amount of power; others never improve enough to gain even a small amount of control of their limbs. When the tumor is in the cervicodorsal region the improvement of the upper extremities may be very marked while that of the lower limbs may be very slight.

The lumbosacral cord is very vulnerable as far as the centers for the bladder and rectum are concerned, and loss of control of urine and feces may persist even after the disappearance of all other symptoms.

From the appearance of the cord at the time of the operation no conclusions can be drawn regarding the amount of improvement that can occur. As it is always inadvisable to handle or even touch a part of the cord that has been subjected to pressure for a long time the operator can seldom determine the exact condition of the affected cord. It is quite astonishing, however, how great an improvement may occur in a cord that appears at operation, to be flattened to a thin tape size. As I have already stated, much greater improvement may be expected in a flattened cord than in one in which there is a deep depression from a small hard tumor (Figs. 7 and 8).

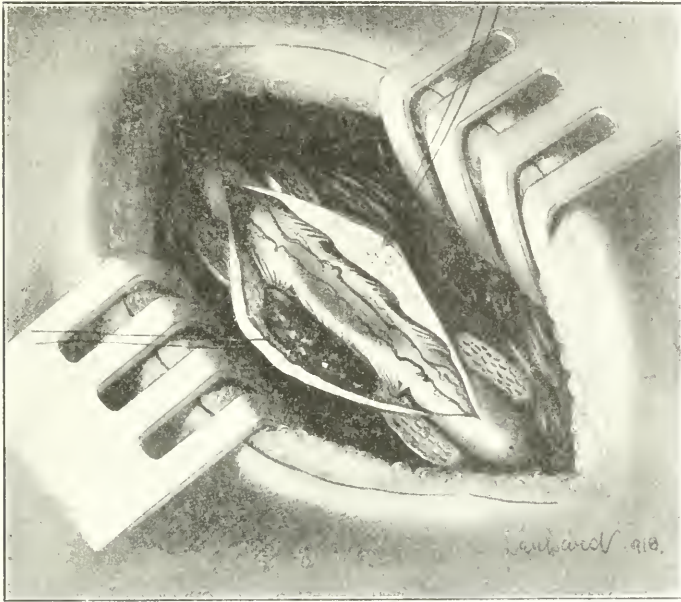


FIG. 7.—E. S. Dural endothelioma which has markedly flattened the cord.

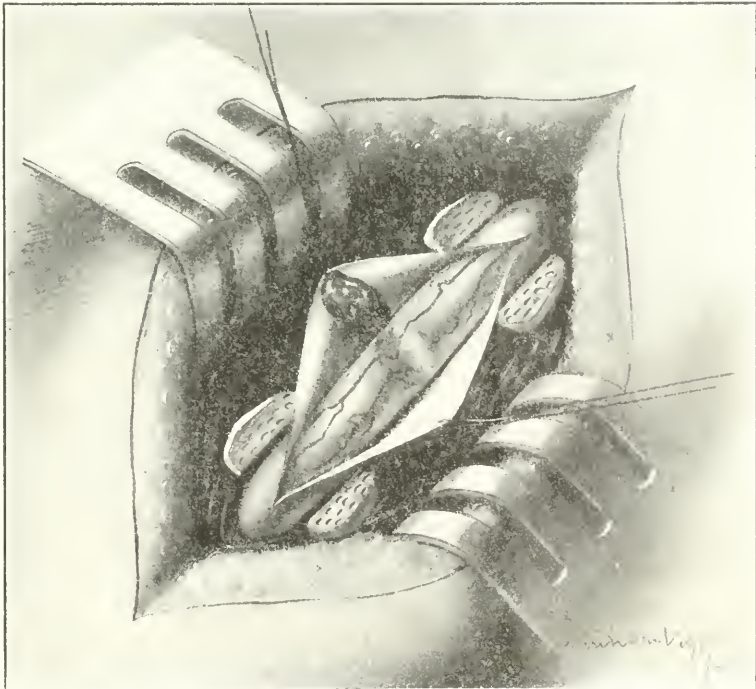


FIG. 8.—Mrs. H. Small dural fibroma which has caused a localized depression in and softening of the cord.

It is never possible to say what improvement will follow the removal of a localized intramedullary growth by the method of "extrusion." We have seen some excellent recoveries but have had many disappointments. The majority of intramedullary tumors are infiltrating in character and the destruction of cord tissue is usually extensive.

What has been said of the tumors that compress the spinal cord holds true, in a general way, for those that develop between the roots of the cauda equina. As the lower end of the spinal canal is

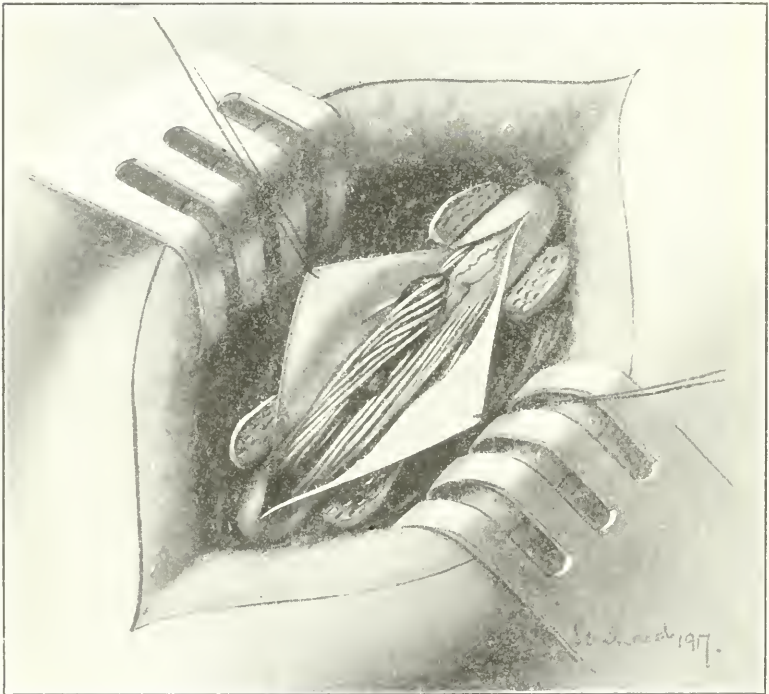


FIG. 9.—Mrs. R. Small tumor, under the left roots of the cauda equina, compressing the conus.

relatively large the tumor must have attained a considerable size before all of the caudal roots are affected. The most frequent form of newgrowth in the caudal region is one which is soft, and which attains a very large size, and is usually firmly adherent to the different nerve roots. To entirely remove these large growths would require the resection of a number of the nerve roots, which is, of course, not permissible or an amount of handling of the roots which would be tantamount to their destruction. Small tumors between the roots of the cauda equina are relatively rare (Fig. 9) and the injury to the nerves can be fully recovered from. It is

remarkable, however, how little sensory disturbance may be caused by the large tumors which so often fill up the entire lower end of the spinal canal and envelop each and all of the nerves of the cauda equina.

CONCERNING DIAGNOSIS. The diagnosis of an extramedullary spinal cord tumor, when the symptoms and signs are well marked, is, in the majority of instances, comparatively easy for those experienced in this field, and most of the patients were sent to us, for surgical interference, with the diagnosis of "cord tumor" already made. The most frequent difficulty experienced was to distinguish between true spinal cord neoplasm and malignant vertebral disease, because malignant disease of the bone may be slow in its development, the onset of the spinal symptoms gradual and the roentgen-ray picture negative. The diagnosis is not difficult if there is a history of primary disease in some other part of the body; but in the cases of primary vertebral disease or at least a disease of the vertebræ in which no primary lesion in any other part of the body can be discovered, the diagnosis is often difficult.

The back of every patient in whom a spinal tumor is suspected should be carefully examined. In patients who are unable to sit up and who have to be turned on the side, we have sometimes found a small swelling to one or the other side of the vertebral spines only after repeated examinations.

Although the spinal cord symptoms which occur with malignant disease of the neighboring bones are usually sudden in their onset and progress within a few days to a complete flaccid paraplegia, the symptoms may develop more gradually. In these patients the differential diagnosis may be difficult. We do not know, in many of the cases, whether the spinal symptoms are due to a toxic or circulatory softening of the cord, because in not a few instances the malignant growth has not made any direct pressure upon the spinal cord.

The diagnosis of "spinal cord tumor" was made more and more early as we gained greater experience with these cases. Many patients had to be watched for months or years before the diagnosis could be made, for a neuralgia has no significance so far as the spinal cord is concerned until some symptoms referable to the spinal cord have appeared. Many of our patients had been, of course, treated for neuralgias or for vertebral diseases for considerable periods, and some had been operated upon for suspected intra-abdominal conditions before the cord symptoms had become manifest.

The diagnosis of "intramedullary tumor" is more difficult, and in many of the patients upon whom a laminectomy for intramedullary disease was performed by us we were uncertain as to whether the disease within the substance of the cord was neoplastic or degenerative.

Of the 67 patients in our series the diagnosis of tumor was made or

suspected 60 times; in the 7 other patients a tumor was considered one of the possibilities. In order to obtain a fair idea of the diagnostic possibilities, however, all of the operated patients should be mentioned in whom a tumor was considered either certain, probable or possible. In all there were 105 patients in this category. In 70 patients the diagnosis of tumor was made or considered probable and in 60 of the patients a tumor was found at the operation. In 35 patients a tumor was considered possible but not probable; in only 7 of these was a tumor found at operation, and 5 of the 7 patients had an irremovable intramedullary growth. The 28 patients in whom a tumor could not be excluded and in whom an exploratory operation was performed, suffered from one of the following conditions: malignant disease of the spine, pachymeningitis, adhesive arachnitis, neuritis of the cauda equina, multiple sclerosis, gliosis, funicular myelitis, abnormal spinal vessels with intramedullary disease. Thus it will be seen that, in our experience, the diagnosis of "spinal cord tumor" was made correctly in the majority of the patients (60 out of 70 cases). When the diagnosis could not be made but a neoplasm was considered possible, though not probable, there was no tumor in most of the patients (28 out of 35 cases).

In the majority of instances the tumor was found at or near the suspected level. Table II shows that in all but three of the patients the tumor was found either at the suspected level or no more than three segments higher or lower than had been diagnosticated. In all of these patient the growth was exposed after the removal of several additional vertebral arches.

TABLE II.

Total number of cases	67
Level diagnosis correct	48
Level diagnosis too low:	
1 segment	8
2 segments	4
3 segments	2
10 segments	2 (removed at second operation). ²
Level diagnosis too high:	
1 segment	1
2 segments	1
6 segments	1 (removed at second operation). ²

² These cases will form the subject of a paper on The False Localizing Signs of Spinal Tumors, which will be published by Dr. I. Strauss and myself.

In one patient the level symptoms pointed to a lesion at the sixth dorsal segment, but the tumor was found at a second operation at the twelfth dorsal segment. In two other patients the diagnosis of a tumor at the level of the twelfth dorsal segment was made. The operation failed to expose the growth. A year or more later, in each patient, there were clear level symptoms in the cervical region,

and in both instances I removed the tumor from the lower cervical region at a second operation.

THE SURGICAL TREATMENT. If an extramedullary tumor has been exposed by laminectomy and incision of the dura its removal does not, in most instances, present any technical difficulties. If the growth lies on the posterior surface of the cord and is not adherent to that structure it can often be "picked out" of the spinal canal with the division of perhaps only a few fine adhesions. If, on the other hand, it lies under a nerve root or in front of the dentate ligament or the cord itself the manipulations must be very carefully accomplished. It is always inadvisable to attempt to pull out a tumor from under a nerve root, as such a procedure might cause serious injury to the cord. Either the nerve root or roots must be carefully raised and pulled apart by fine strabismus hooks, or if sufficient room cannot be gained the roots must be divided.

Similarly the surgeon should never attempt to pull out a tumor from under a slip of the dentate ligament. The slip should be divided and retracted in order to expose the newgrowth. When a tumor is to be removed from in front of the cord the following procedures are of value: By the division of one or two slips of the dentate ligament and of one posterior nerve root (if necessary) the cord can be pulled well to one side. This should be done with forceps which grasp the slips of the dentate ligament which have been divided and not by direct pressure upon the cord. The operator should never make the attempt to pull the cord to one side by means of traction on one or more nerve roots. A pull on a nerve root sufficient to draw the cord to one side is almost certain to injure the cord itself.

Another important detail in the exposure and removal of tumors which lie in front of the cord is to remove much more of the laminae on one or other side, so that the access to the front of the cord from that side is made more direct.

If the neoplasm is found to be closely adherent to the cord the greatest possible gentleness should be used in separating it from that structure. Tumors which have originated from the pia mater on the cord are sometimes so firmly adherent that in their removal a small layer of cord tissues would come away with the growth. If the adhesion is a very firm one it is preferable to leave behind a small piece of the capsule of the growth.

If the neoplasm is not found at the exposed level a careful search must be made for it. The appearance of the veins on the posterior surface of the cord is very characteristic when there is an obstruction to the return flow of blood at a higher level. In addition a probe should be carefully passed upward and downward on the posterior and anterior aspects of the cord. An elastic resistance is often felt when the end of the probe impinges upon a tumor higher up or lower down than the exposed area. Mistakes may, however, occur

when the end of the probe is caught in a nerve root, in an adhesion between the arachnoid and the dura or is obstructed by a swollen cord or one of the normal curves of the vertebral column. If there is no escape of cerebrospinal fluid from above and such an elastic resistance to the progress of the probe is encountered, especially if there is a venous congestion of the cord, a tumor at a higher level than that exposed is very probable.

OPERATIVE RESULTS. In order to obtain an adequate idea of end-results a careful study of each case is necessary. Many of our patients have recovered completely and have remained well, others have retained symptoms that were more or less disturbing to them; still others have remained subjectively well, although examination showed that some neurological abnormalities had persisted. Then there were the patients in whom, on account of long duration of the disease or of advanced cord compression, little or no improvement followed the removal of the tumor. Finally there was the group in which removal of the growth could not be accomplished. Some of these patients have been much relieved by the decompressive effect of the operation, while most of them were of course not improved. We have been able to "follow up" a large number of our patients and shall, in the near future, report in detail on our "end-results."

In this paper I shall speak only of operative results as summarized in the following table:

TABLE III.

Relation of tumor to cord.	No. of cases.	Tumor removed.	Tumor partly removed.	Tumor not removed.	Deaths.	Recovery.	Per cent.
Extramedullary	31	31	—	—	2	29	=94
Cauda equina	11	1	8	2	2	9	=82
Extradural	7	3	1	3	1	6	=86
Intramedullary	18	4	2	12	2	16	=89
Totals	67	39	11	17	7	60	=90

Many physicians still believe that the operation of laminectomy is a very dangerous one, but the statistics of those who have had experience in this special field show that the danger of a spinal operation is not very great. Thus of the last 200 laminectomies performed by the writer, 12 cases ended fatally, a mortality rate of 6 per cent. The mortality of the operation of laminectomy and removal of a spinal cord tumor should not be large. Of 67 patients in our series, 7, or 10.4 per cent., died after the operative interference; in the operations for extramedullary tumors there was a mortality of 6 per cent.

Two patients with extramedullary cord tumors died four days after the removal of the tumor; an old diabetic (sugar-free before the operation) died on the fourth day in diabetic coma; the other patient was a very stout woman, aged sixty-four years, who succumbed to an ether pneumonia on the fourth day after the operation. Two patients with tumors of the conus and cauda equina died, one

of them five days after operation from necrosis of the wound and sepsis, the other four days after the surgical interference in coma with a hemorrhagic nephritis. The fifth patient was a child of four years, with a large extradural sarcoma which was found to be an extension of a large malignant growth of the right chest. The patient died in shock twenty-four hours after the removal of the growth in the spinal canal. The sixth and seventh patients had high cervical intramedullary tumors. One patient had an intramedullary infiltrating glioma in the upper cervical cord that was an extension downward of a tumor in the posterior cranial fossa. The growth could not be removed and death occurred on the third day from respiratory paralysis. The other patient was a woman with respiratory and cardiac symptoms from a localized intramedullary tumor of the third to fifth cervical segments. This was one of our earliest cases, and after incision of the cord I removed the tumor at the first operation. The patient died from respiratory paralysis two hours after the operation.

A study of these fatalities will show that we have operated upon some patients in whom surgical interference should have been refused; they were operated upon in the beginning of our experience with spinal surgery. It was certainly hopeless to attempt to remove an infiltrating growth, such as in Case VI, or to remove in one stage an intramedullary tumor, as in Case VII. The child with an extension into the spinal canal of a newgrowth in the thorax should not have been operated upon.

The above facts are stated, not with the object of explaining away the mortality rate of 10 per cent. in our operations for spinal cord tumors, but to show that the fatalities after these operations, if the cases are properly selected, should be no larger than 6 per cent. In the future still better results should be obtained.

BRACHIAL BIRTH PALSY: A PSEUDOPARALYSIS OF SHOULDER-JOINT ORIGIN.¹

BY T. TURNER THOMAS, M.D.,

PHILADELPHIA.

GENERAL CONSIDERATIONS.

IN 1907 in an adult case of traumatic brachial paralysis with ankylosis of the shoulder-joint following an injury about a year and a half before, breaking up of the ankylosis under ether and the use of forced exercises by the patient resulted in about three months in the return of normal power to the whole limb which

¹ Read before the College of Physicians of Philadelphia, October 1, 1919.

has remained unimpaired since. This has been followed by many similar cases of varying grades of severity, in most of which forced exercises without a preliminary breaking up of the ankylosis under ether sufficed to restore the normal motion to the shoulder and power to the limb. The treatment was so simple and the paralysis usually so fleeting that records were kept of only a small number of special cases. In 1909, in a more severe type of traumatic brachial paralysis, with flail shoulder-joint in an adult, transferred to me at the Philadelphia General Hospital from the service of Dr. J. Chalmers Da Costa, by operation the normal shoulder-joint firmness was restored and by forced exercises the operative stiffness or ankylosis afterward removed. In about four months the patient had a normal arm and has had it since. I have now had 18 similar cases; 12 have been operated on. In 9 the paralysis disappeared and in 2 more it is disappearing. In one case death from lung involvement occurred too early to permit recovery from the paralysis. In 1910, in a boy, aged seven and a half years, with a brachial birth palsy, I found a hitherto undiscovered posterior shoulder subluxation of the same side. A complete paralysis at birth had practically disappeared, a considerable wrist-drop remaining, but the limb was much shortened and crippled from the persistence of the old shoulder-joint displacement. Operative reduction of the dislocation was not completely successful, but the wrist-drop was much improved as well as the function of the whole limb. This was the first time this operation had been done for this condition, but it has already become the prevailing operative treatment for it. I have now had 44 cases of brachial birth palsy and am satisfied that these as well as the above adult cases have been pseudopalsies, due to inclusion of the brachial nerves in an axillary inflammation, consequent upon an injured shoulder-joint and not true paralyzes from injuries of the brachial plexus. Those interested will find a summarized discussion of this whole subject with the associated literature in the *Journal of the American Medical Association*, 1914, ii, 1018. It is not intended here to infer that the paralysis is not real and extensive and that the nerves are not involved, but merely that the paralysis is a pseudoparalysis in the sense that it is only temporary in the great majority of cases. An explanation of the temporary nerve involvement is offered, but even this is not insisted on. It is merely supported until somebody else offers a better explanation. What is insisted on, however, is that the primary and essential cause of the trouble in most cases is in the shoulder-joint, and that when that is removed early enough we need not be much concerned about the paralysis. That will then take care of itself. What we need most in the obstetrical cases is skillful attention to the shoulder at birth by the accoucheur, but we are probably a long way from this now.

It is manifestly impossible for this new and radical view to make headway without controversy against the universally accepted contrary theory, that of injury to the brachial plexus. The recent work of J. J. Thomas and J. W. Sever, in support of the plexus theory, directly challenges the shoulder-joint origin. They published the results of their work in three papers, all covering essentially the same ground, to which I shall refer when necessary, for the sake of brevity, as the orthopedic,¹ pediatric² and neurological³ papers. The object of their work is seen in the following (pediatric): "Up to within a year or so most of us were reasonably content to accept the theory that the paralysis in these (obstetrical) cases was due to a stretching or tearing of some of the roots of the brachial plexus, due to a forcible separation of the head and shoulders during labor. Other theories have been discussed and have been given some credence, but recently a new one has appeared. It seems that it is about time for us to take account of stock and see which of these various ideas which have been advanced are reasonable and based on pathological findings, and clinical facts." Their essential conclusion is as follows: "There is no evidence from our experimental work or clinical observations to support the theories of Lange and T. Turner Thomas that the primary cause of obstetrical paralysis lies in an injury of the capsule of the shoulder or dislocation, with secondary damage to the nerve trunks."⁴ They admit that a few cases of shoulder-joint origin may simulate obstetrical paralyses, but claim that these are readily distinguishable.

When it was decided that I would assume the responsibility of opposing the then universally accepted plexus rupture theory and attempt to substitute a shoulder-joint origin, there was no reason to suspect it would soon be necessary to maintain priority for this view. In this connection it now becomes necessary to point out a certain confusion of facts, particularly in the papers signed by Sever alone. I am credited with only one paper, and this is given two dates of publication, 1913 and 1914. Lange's single paper is credited to 1912 and 1913. Notwithstanding these dates, Sever says: "T. T. Thomas has fallen back on the old Lange theory that the injury to the plexus is secondary to an injury to the joint capsule at birth and that the paralysis is due to an exudate which surrounds and compresses the plexus." In the neurological paper, signed by Thomas and Sever, I am credited with six papers and am here given credit for priority over Lange by two years, my first paper being dated 1910 (it was read in 1910) and Lange's 1912, and yet the following statement appears in this paper: "T.

¹ Sever: *Am. Jour. Orthop. Surg.*, 1916, xiv, No. 8.

² Sever: *Am. Jour. Dis. Child.*, 1916, xii, 541.

³ Thomas and Sever: *Jour. Nerv. and Ment. Dis.*, 1916, xlv, 289.

⁴ Thomas and Sever: *Jour. Am. Med. Assn.*, 1916, i, 206.

Turner Thomas was, perhaps, the first advocate of this theory in this country." I would state the facts as follows: The first mention in the literature of the shoulder-joint origin of traumatic brachial paralyses in adults and in children at birth and the first suggestion that the basic primary lesion was a laceration of the joint capsule appeared in my paper of the January, 1911, issue of the *Annals of Surgery*, while this is my sixth paper on the subject. Lange's first and only paper on obstetrical paralysis appeared in the latter part of June, 1912.

The few writers who have taken up the Klumpke,⁵ lower arm, type of traumatic brachial paralysis in support of the Duchenne-Erb, upper arm, type have added to the difficulties in the solution of an already troublesome problem. There is distinct evidence that most of them have not studied Klumpke's paper. The general tendency has been to avoid this phase of the subject, and with good reason. Madame Klumpke did not report any personal experience with obstetrical paralysis, but referred to two cases reported by Seeligmüller. Her paper was based on one personal adult case of total, flaccid, brachial paralysis of motion and sensation together with a collection of similar cases from the literature. A sharp distinction should be made between this and the Duchenne-Erb type of paralysis. Klumpke saw the difference which must impress anyone who will study the two groups of cases. In the Duchenne-Erb there is essentially no disturbance of sensation, although all cords of the brachial plexus are mixed motor and sensory nerves; the paralysis of motion gradually disappears completely except occasionally for some atrophy and weakness, due to a severe restriction of motion at the shoulder-joint, sometimes at the elbow; and there is a practically constant but varying grade of such joint ankylosis. Klumpke's case was an adult and the cases she collected from the literature like it were adults. Note how the condition she found in her own case differs from that found in the Duchenne-Erb type: Sensation is completely and permanently lost except for some variation in its upper limiting border; the paralysis of motion is likewise complete and permanent; and there is no report of ankylosis at the shoulder. The Duchenne-Erb is a temporary or pseudoparalysis, the Klumpke a permanent or true paralysis. Klumpke's chief interest and study was in connection with oculomotor phenomena, particularly inequality of the pupils, and it was because of similar phenomena in Seeligmüller's two cases that she included them with her adult cases. Inequality of the pupils has not been reported often in connection with obstetrical paralysis and not with much positiveness and detail when it has been. I cannot say that it has attracted my attention in any of my cases. I have observed asymmetry of the face but have attrib-

⁵ Rev. de méd., 1885, v, 591 and 739.

uted it to a sympathetic or associated atrophy on the side of the brachial paralysis. I have seen the same side of the chest much atrophied as well as the face.

The fact that in the great majority of obstetrical paralyses the paralysis gradually disappears until it cannot be recognized explains why reports of the condition in adults are so rare. I have never seen such a report, but I have seen two cases of rather a severe grade in adults. One was an orthopedic surgeon who very kindly called on me and gave me the privilege of examining the arm. He had a posterior subluxation of the shoulder-joint, a marked bending downward and forward of the acromion, which was shown well by the roentgen ray, and still had a considerable limitation of movement in this joint. He said the condition had been much more severe in his younger years, but there was at the time I saw him no evidence of paralysis. In addition to the absence of paralysis he furnished another good reason why we do not recognize the condition in adults. He could not afford to permit his present and prospective patients to know that he was crippled and unable to help himself. He added, also, that, so far as he knew, none of his patients or colleagues ever suspected the condition. The second case was a pupil nurse who seemed to have no trouble in performing her duties. She had no paralysis but had some atrophy from the limitation of movement at the shoulder.

SUPPORT FOR THE SHOULDER-JOINT PATHOLOGY. The temporary or pseudoparalysis, the practically constant preservation of sensation and the practically constant limitation of shoulder movement, which seems to be readily accounted for by the compression of the shoulder by the maternal pelvis during delivery, led me to suggest that the joint injury was primary and the paralysis secondary to it from inclusion of the branches of the brachial plexus in the axillary inflammation consequent upon the joint injury. A non-traumatic inflammation of the joint could produce a similar result. Since I never considered it justifiable to expose the nerves in any of my cases I have been compelled to offer the postmortem and operative evidence of others. Delbet and Cauchoix⁶ collected 33 cases from the literature of brachial paralysis in adults following dislocation of the shoulder and added 2 of their own, in which the nerves were exposed at autopsy or operation, usually in the axilla. No rupture was found, but the nerves were embedded in cicatricial tissue, inflammatory tissue or bloody extravasation. Lange⁷ exposed the axillary nerves in a case of obstetrical paralysis and found the cause of the paralysis to be the embedding of the nerves in dense connective tissue for an extent of about 4 cm. In 81 cases of obstetrical paralysis in which the brachial plexus was exposed,

⁶ *Rev. de chir.*, 1910, xxx, 673.

⁷ *München. med. Wechschr.*, June, 1912, No. 26.

Wyeth and Sharp⁸ found that the "usual lesion was a dense connective-tissue formation choking the plexus and thus impairing its function." Most others who have operated on the plexus in obstetrical paralysis have interpreted these cicatricial conditions as being due to rupture of the brachial plexus. Ashhurst⁹ says: "The descriptions of what has been found at operation soon after birth are so vague that not much reliance can be placed on such observations; this vagueness probably is due to the impossibility of telling, even with the nerves exposed to view, how much they were damaged. In cases operated on months or years after the injury occurred the extent of the scar tissue and the difficulty of the dissections render such observations also of limited value." Eversmann¹⁰ reported the autopsy findings in a case two and half months after birth. The only lesion discovered was an induration, with thickening at the junction of the fifth and sixth cervical roots of the brachial plexus, for $\frac{1}{2}$ to $\frac{3}{4}$ cm. One could hardly accept these findings as proving a nerve rupture, although they have been widely quoted to prove such an injury.

Stransky¹¹ quotes Rouland as reporting an autopsy on a case of obstetrical paralysis which died on the tenth day. The nerve findings were negative. It is probable there is not a case of obstetrical paralysis on record in which a frank, recent rupture of any of the cords of the brachial plexus has been found at operation or autopsy. Probably the only case on record with an autopsy soon after birth showing evidence of injury is that of Danyau,¹² who did not find nerve rupture but bloody extravasation around the plexus. He regarded it as evidence of injury of the plexus by forceps, and most of the writers who have since quoted the case agreed with him. Seeligmüller,¹³ who was contemporary with Danyau, Duchenne and Erb, and one of the most quoted writers on this subject, thought that the bloody extravasation came from injury of the surrounding tissue by the forceps. He quotes the findings by Fritsch in autopsies on children born by the breech of bloody extravasations under the skin and in the muscles. He believed with Fritsch that such blood could alone cause paralysis by pressure on the nerves, so that with the disappearance of the blood the paralysis would disappear. Fritsch found in one case two days after a difficult delivery of the head a 5 cm. wide hematoma near the lower end of the sternomastoid, the disappearance of which was followed by disappearance of a paralysis of the corresponding arm.

⁸ Surg., Gynec. and Obst., 1917, xxiv, 34.

⁹ Ann. Surg., 1917, lxxviii, 25.

¹⁰ Arch. f. Gynec., lxxviii, p. 143.

¹¹ Centrallbl. f. d. Grenzgeb. d. Med. u. Chir., 1902, v.

¹² See Duchenne, l'Electrisation, 1872, pp. 353-357.

¹³ Berl. klin. Wchnschr., 1874, p. 510.

SEVER'S CAPSULE INJECTIONS AND THE DUCHENNE-ERB THEORY. The suggestion that the paralysis is due to inclusion of some or all the branches of the brachial plexus in the axillary inflammation consequent upon a shoulder-joint injury is combated by Sever as follows (pediatric): He injected the shoulder-joint of several newborn infant cadavers with methylene-blue and then made an opening in the anterior part of the capsule of the joint to prove that the exudate following a dislocation or sprain of the shoulder-joint would not extend to the brachial plexus above the clavicle. In answer to this I would merely say that if the ecchymosis and exudate from a dislocation of the shoulder-joint, as not infrequently happens, extravasates to the elbow and hand, it will surely go a few inches above the joint to the brachial plexus, particularly in a newborn infant occupying generally the recumbent position. A discussion of the following quotation from Sever could be of very much importance, because it concerns the most vital part of the whole question. "This (the surrounding and invasion of the axillary nerves by the methylene-blue) would in life lead to a paralysis of the whole arm at and below the joint (shoulder), but would in no way affect the nerves above the clavicle, and in no case would there be the typical picture of obstetrical paralysis, *i. e.*, paralysis of the fifth and sixth cervical. As I have stated before, why the exudate should leave the nerves alone in immediate proximity of the capsule and seek out Erb's point, the junction of the fifth and sixth cervical segments, at least two or three inches above the clavicle, Lange and Thomas and others have not made quite clear." The emphasis here should be laid on the fact that Sever accepts without reserve the localization of the lesion at Erb's point. Such unreserved acceptance is very rare in the literature, today, although a few years ago it was almost universal. In a discussion of this subject with an eminent surgical friend in the spring of 1914, he said: "Am I to understand that you do not accept the C V and C VI (Erb) theory?" On my replying in the affirmative he said: "I am amazed! I did not think that anyone doubted that." So far as the literature shows, that was the attitude of probably the whole profession a short time before, but it (Erb theory) has lost a few supporters since.

The amazing thing is that so many writers have accepted and so few have proved it. What is this Duchenne-Erb idea and upon what kind of evidence does it rest? Duchenne,¹⁴ in four infants a few weeks old, localized the paralysis by *electrical reactions* in every case, without exception, to the deltoid, biceps, brachialis anticus and infraspinatus. This was in 1872. Erb,¹⁵ in 1874, in four adults, localized the paralysis by electrical reactions without

¹⁴ Loc. cit.

¹⁵ Naturhistorisch. medicin. Verein zu Heidelberg, 1874, No. 1, 130.

exception to the deltoid, brachialis anticus and biceps, usually to the supinator longus and sometimes to the supinator brevis, in one case to the supply of the median in the forearm and hand. In one case of obstetrical paralysis, two months old, he found that "The exact observation, which naturally gave considerable difficulty, showed that the deltoid, biceps, brachialis anticus (probably also the supinator longus), were completely paralyzed and that the infraspinatus was also probably paralyzed." Erb's particular contribution consisted in the fact that he localized the lesion to the junction of the fifth and sixth cervical roots of the plexus. We are confronted at once with the difficulty that the two differed in their localization of the paralysis, but this does not seem to have attracted particular attention. The most characteristic feature of the paralysis is the internal rotation. It is of interest that Duchenne accounted for the internal rotation from the shoulder down and Erb from the elbow down, Duchenne attributing it to paralysis of the infraspinatus and Erb to paralysis of the supinators of the forearm. Obviously the only way by which their work can be corroborated is by finding the same specially localized paralysis in the same way as they did—by *electrical examination*. There can be no substitute for this evidence. To what extent has this been done since the reports of Duchenne and Erb forty-seven and forty-five years ago? A satisfactory answer to this very important question would probably be impossible because of the very extensive literature that has accumulated and the difficulty of avoiding errors in searching it. Thomas and Sever collected the literature since 1902 and referred to that collected by Stransky up to that time, in this way covering the whole ground. All of this literature has been scanned with the purpose of finding cases in which the electrical reactions obtained by Duchenne and Erb were confirmed. While one hesitates to give the results because of the possibilities of error and the impossibility of gaining access to some papers, particularly to the theses, a strong suspicion was developed that no matter how careful the investigation very few such cases can be found. Gowers,¹⁶ in 1888, in a clinical lecture referred to a case of obstetrical paralysis examined before the same class a few weeks before in which the electrical reactions characteristic of degeneration had been found in the deltoid, biceps and supinator longus. This is the closest corroboration of Duchenne and Erb that I succeeded in finding, and here there is no mention of the brachialis anticus which was included by Duchenne and Erb. Shoemaker¹⁷ is one of the most quoted supporters of this theory. In the first of his two cases, in the first few days, the right arm hung in internal rotation, motionless except for slight extension and

¹⁶ Lancet, April 14, 1888, p. 709.

¹⁷ Ztschr. f. Geburtshilfe und Gynäk., 1899, xli, 33.

flexion of the fingers. In four to six weeks the power of the other muscles had so improved that a pure Duchenne paralysis had developed which was characterized by involvement of the supra- and infraspinatus, deltoid, biceps and supinators. His interpretation of a "pure" case is evidently open to question. Nor did he make any mention of the use of electricity. Of his second case he said "exact examination shows that the following muscles exhibit delayed development: supra- and infraspinatus, deltoid, biceps, triceps and supinators," surely not a pure case. He quotes Roulland (*Thèse de Paris*, 1887) as reporting a case spontaneously born with a typical Duchenne-Erb palsy (supra- and infraspinatus, deltoid, triceps and brachialis anticus). Here there is no reference to electrical reactions nor to palsy of the biceps, while the supra-spinatus and triceps, not mentioned by Duchenne or Erb, are included in the paralysis. Hochsteter,¹⁸ in 1893, reported a case in which "electrical examination by Goldscheider at the end of the third day showed no response of the nerves on both sides, to the constant or indirect current, on the other hand the arm muscles on the paralyzed as on the sound side were brought directly to contraction by both currents." These few cases represent merely a crude effort to turn light on a phase of this discussion that much needs it, and if it results in similar efforts by others it will have served its chief purpose. Unless someone else can do better than this we must assume that the findings of Duchenne in four cases and Erb in one case of obstetrical paralysis represent the only scientific evidence upon which the Duchenne-Erb etiology for this condition is resting today, *i. e.*, the originators of the theory have not been corroborated.

The number of cases reported has increased rapidly in the last few years, but those in which the electrical findings are reported still remain conspicuous by their absence. The failure to find such cases in the literature is strongly corroborated by the following: Fairbanks, in 1913, reported a personal experience of 40 cases, probably the largest up to that time, and supported the brachial plexus theory. He said that electrical examinations are not necessary before the end of the second month, the use of an anesthetic being essential; but by this time the case will probably show definite signs of recovery, so as to render electrical examination unnecessary. Thomas and Sever report a personal experience of 471 cases, by far the largest up to the present, and, perhaps, as large as that of all other writers put together. Sever says of these cases "electrical reactions have not been carried out, for this examination would mean anesthesia, which did not seem justifiable when one already had all the necessary data." We are looking now for corroboration of Duchenne and Erb, and we have here

¹⁸ Berl. klin. Wehnschr., 1893, xxx, 1016.

what amounts practically to a confession that it is not obtainable. There is nothing in the articles of Duchenne and Erb to indicate that they found anesthesia necessary for their electrical examinations. Why should it be necessary for ours? Does this not indicate something radically wrong with their method of electrical examination or with ours? Of what value is it to us that Duchenne forty-seven years ago in four cases, and Erb, forty-five years ago in one case, found these electrical reactions if we cannot find them in any of our hundreds of cases today? It seems to me that those who accept the Duchenne-Erb theory carry a heavier responsibility than those who reject it.

If one may judge from the apparent lack of familiarity of most writers on the subject with the original articles of Duchenne and Erb and the difficulty I experienced in gaining access to them, very few have consulted them. This probably has had something to do with the widespread and unchanging faith that has grown up around them. There has been too much agreement with and dependence on what they found. Sever says that the results of his methylene-blue injections into the shoulder-joint indicated that in life we should have "a paralysis of the whole arm at and below the joint (shoulder)," but that we do have instead a localized paralysis of the Duchenne-Erb type. My experience has led me to the reverse opinion, that we do have the kind of paralysis suggested by Sever's experiments, soon after birth, and do not have the Duchenne-Erb localization, soon after birth or at any other time. I saw 5 cases within eight weeks after birth. One of the 5 had, at six weeks, made a rapid recovery and was moving all parts of the limb, although not normally. Later it made a complete recovery. Dr. L. C. Peter, a neurologist, saw the patient soon after birth and then found a complete paralysis except for slight movements of the fingers. In 1 case seen five days after birth there was not observed a single movement in the whole limb, not the slightest in any of the fingers, but occasionally the child would move the limb as a whole at the shoulder. In the other 4 cases there were very slight movements of the fingers, but of no other part of the limb. These findings are in perfect accord with the results of Sever's experiments.

ERB'S LOCALIZATION. Probably the most striking features of Erb's paper are its positiveness and the dogmatic character of its clinical findings and conclusions, which allow little else to the reader than to accept or reject them. The result has been so one-sided that one will probably look in vain for any attempt at question concerning them. His localization of the lesion to the junction of the fifth and sixth cervical roots of the brachial plexus is based essentially on his findings by electrical examination in the four adult cases. His one obstetrical case was evidently employed to show that this special localization discovered by Duchenne in

his obstetrical cases was the same as in his (Erb's), adult cases, so that one wonders how the modern supporter of the Erb C V and C VI theory can accept this special localization for the obstetrical cases without accounting for the adult cases in present-day practice. For many years it was accepted for the adult cases, but one looks almost in vain today for any mention in text-books or the literature of this condition in adults. So far as it has been corroborated by electrical examinations in adults it has never had a strong position, according to my investigations. Taylor and Casamajor (*Annals of Surgery*, November, 1913, p. 577) reported 6 adult cases in connection with 4 of which very incomplete electrical reactions were given. They do not corroborate Erb's or Duchenne's findings. Remak¹⁹ in 1877, Hoedemaker²⁰ in 1878-1879, Bernhardt²¹ in 1882 and Nonne²² in 1887 reported cases in which they found this specially localized paralysis of Erb by electrical examination, but the localization was far from being as precise as in Erb's original paper. It is of some interest to note that Remak was a pupil of Erb, that one of Hoedemaker's 2 cases occurred in the private practice of Erb and that Erb made the electrical examination in Nonne's one case. I found only one other adult case reported in which a similar paralysis was established by electrical examination, but the report was so brief and casual that one hesitates to use it as corroboration. In my opinion Erb's paper is open to at least one serious criticism. He localizes the lesion to the junction of the fifth and sixth cervical roots of the plexus. The fibers to many other than his paralyzed muscles pass through this junction, but he says that "In all four (adult) cases, without exception," the lesion involves the fibers to the same four or five muscles, all the other fibers escaping every time. Now in Case I he accounts for this particularly localized lesion by a traumatic neuritis of the brachial plexus from carrying a heavy load on the head. In Case II, he accounts for the same lesion by a "traumatic lesion of a part of the brachial plexus" from a fall down stairs on the outstretched left hand and simultaneously striking with the left shoulder against a wall. In Case III he accounts for it by a "neuritis of a certain portion of the brachial plexus" of unknown cause. In Case IV we are told that a cancerous involvement of the supraclavicular lymph nodes, the patient dying in a few weeks from carcinomatosis, produced pressure on the brachial plexus only at Erb's point. It does not seem to me that such a precise localization of the lesion would be accepted today on such evidence.

Every surgeon knows there is a large number of cases of weakness or palsy of the arm following injury of the shoulder, the

¹⁹ Remak: Berl. klin. Wehnschr., 1877, xiv, 116.

²⁰ Arch. f. Psychiat. u. Nervenkrankh., 1878-9, ix, 738.

²¹ Ztschr. f. klin. Med., 1882, iv, 415.

²² Deut. Arch. f. klin. Med., 1887, xl, 62.

pathology of which has never been satisfactorily established. Some see them as paralyses, others only as stiff and painful shoulders of uncertain cause. It is generally understood that dislocations of the shoulder are frequently associated with the severe cases. It is very likely that the Duchenne-Erb type of paralysis resulted from one of the efforts to solve the problem involved. Schulz,²³ in 1908, reported a study of the late results in fifty-four uncomplicated dislocations of the shoulder and found varying grades of brachial palsy in 75 per cent. of them, and in most of the others there was some diminution of strength. He accounted for them by cicatricial contraction of the joint capsule and surrounding tissues. The outstanding fact in connection with these cases is that there was no nerve complication in any at the time of the dislocation. In the July number of *Surgery, Gynecology and Obstetrics* there is an abstract of a paper by Korteweg²⁴ on "The Results of Dislocation of the Shoulder and its After-treatment." He reviewed 845 cases. The abstract says: "For the diagnosis of a nerve paralysis the author demands the presence of disturbances of sensation and the complete or partial reaction of degeneration." We can only infer that "nerve paralysis" applies here to paralyses due to nerve injury and that Korteweg must have found some that were not in this class. I believe that his diagnostic rule will some day be applied to the obstetrical paralyses by the profession generally and that the Duchenne-Erb theory will fail to withstand the test.

PROGRESS OF SHOULDER-JOINT THEORY. Attention has already been called to the support which the pathology of a shoulder-joint injury in its etiological relationship to these cases has obtained in the literature. The theory of a shoulder origin has gained rapidly in the last few years, and it has had occasional support from the beginning. In his first article (1861) Duchenne attributed obstetrical paralysis chiefly to the associated posterior subluxation which he believed occurred at birth (see Fig. 1). Injury of the brachial plexus also contributed to the paralysis in his opinion. In his second article (1872) he reported 4 cases without dislocation in which he attributed the paralysis entirely to injury of the plexus. The profession afterward practically ignored the dislocations for many years, and during the last fifteen years, when they have been forced upon the attention of the profession again, the supporters of the plexus theory have accounted for them as a secondary development of the paralysis from the plexus injury. Erb, who reported only 1 case of obstetrical paralysis, thought careful examination would show the dislocations to be few in number. Seeligmüller says that these paralyses in the newborn are frequently complicated by fractures and dislocations and that these compli-

²³ Deutsch. Ztschr. f. Chir., 1908, lx, 333.

²⁴ Zentrabl. f. Chir., No. 46, p. 926.

cations have been completely overlooked in many cases. He saw 1 case with an undoubted dislocation of the humeral head into the infraspinous fossa. He says that Smellie (who was the first to report obstetrical paralysis in 1768) reported several cases of persisting arm paralysis, due to dislocation intrapartum. Dauchez²⁵ recognized "obstetrical pseudoparalysis," in which paralysis is simulated by a unilateral or bilateral dislocation of the upper extremity. Küstner,²⁶ in 1889, attracted much attention by his

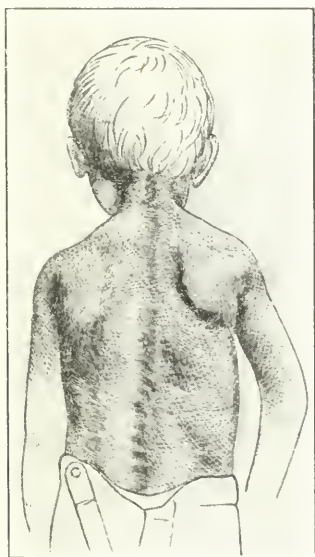


FIG. 1



FIG. 2

FIG. 1.—Duchenne's illustration of his case of obstetrical paralysis with posterior subluxation of the shoulder-joint. The associated paralysis was attributed chiefly to the dislocation which was accounted for by the manipulations of the accoucheur at birth.

FIG. 2.—One of the author's cases with a severe degree of posterior subluxation of the shoulder-joint. The prominence of the humeral head is about as noticeable and there is the same internal rotation of the whole limb and flexion of the elbow, and almost the same prominence of the angle of the scapula, as in Duchenne's case (Fig. 1) The plexus theory supporters, today, say the dislocation is secondary to the paralysis from injury to the plexus.

contention that these obstetrical paralyses were due to injuries of the upper epiphysis of the humerus and the German surgeons who today find the same lesion are probably influenced by his work. The roentgen ray in those cases in which ossification has advanced far enough prove conclusively that the deformity is due to dislocation, not to displacement of a separated epiphysis. B. Sachs²⁷ said, in

²⁵ Ann. de Gynecol., 1891, xxxvi, 300.

²⁶ Handbuch der Geburtshilfe, p. 301.

²⁷ Jour. Nerv. and Ment. Dis., 1904, xxxi, 670.

1904: "If many cases were examined soon after birth there might be found a distinct subluxation of the head of the humerus, probably below the deltoid, which might possibly be identified with Erb's palsy; therefore, all cases of obstetrical palsy were not Erb's palsies." Whitman, in a personal communication in 1914, recognized in addition to the common cases with posterior luxations of the shoulder: (1) True congenital luxations of the shoulder (rare); (2) obstetrical luxations at birth usually with paralysis;



FIG. 3.—Obstetrical paralysis without dislocation, five days after birth. Not the slightest power in any of the muscles of the limb. Today, there is clearly power in all the muscles and the patient elevates the whole limb forward to the level of the shoulder.

(3) fractures of the humerus at birth at any point, rarely with displacement of the epiphysis of the head (may or may not be accompanied by paralysis); (4) in a large proportion of the ordinary cases of obstetrical paralysis there are evidences of injury of the shoulder of the nature of strains or sprains, as shown by sensitiveness to movement and pressure. Lange, in 1912, said that most of the obstetrical paralyses were due to lacerations of the capsule of the shoulder-joint. Platt,²⁸ in 1915, favored the plexus theory for

²⁸ British Med. Jour., May 8, 1915, p. 793.

most cases, a primary injury of the shoulder-joint or upper humeral epiphysis for some cases, but treated only the shoulder ankylosis which he found in all cases. Vulpius,²⁹ in 1914, ascribed these cases to epiphyseal injuries and found by exact examination that there was no real paralysis or, at least, it was not at all prominent. Gaugele,³⁰ in 1914, said that most cases were pseudopalsies, due to distortions of the shoulder-joint, with injuries of the capsule and other soft tissues and confined his treatment to the shoulder-joint. Peltsohn,³¹ in 1914, said that most obstetrical palsies are due not to injuries of the brachial plexus, but injuries of the upper humeral epiphysis. Van Neck,³² in 1912, said that tears of the shoulder capsule and injuries of the upper epiphysis of the humerus simulate obstetrical paralysis. G. G. Davis,³³ in 1916, said that "there is primarily an injury of both nerves and articular structures." He also said: "The restriction of external rotation of the humerus is marked in these infants only a few weeks old," and that "The presence of restriction of movements a few weeks after birth is proof positive of periartritic lesions." His treatment is confined to the restriction of movement at the shoulder-joint, the elbow-joint and forearm requiring attention in some cases. Ashhurst says: "All the muscles most constantly paralyzed are supplied by nerves which pass very close to the shoulder-joint, and, *ipso facto*, are liable to injury; whereas the muscles which habitually escape paralysis are supplied by nerves which at no part of their course come into close relation with the shoulder-joint or the bones which compose it. This seems to bring us very close to the theory of Thomas and Lange that the primary lesion is in the shoulder-joint and that involvement of the nerves occurs secondarily. It is indeed a question in my own mind whether this is not the most acceptable theory for the majority of cases."

CADAVER EXPERIMENTS ON THE BRACHIAL PLEXUS. In the last analysis the Duchenne-Erb theory must rest upon corroboration and the only kind of corroboration that will avail will be to find in our cases what they found in theirs, the proof of the definitely localized paralysis by electrical examinations. What are the other "necessary data" upon which Sever depended? That resting upon the interpretation months or years after birth of the adhesions and nerve thickenings found at operation or autopsy and the experimental data. The operative and postmortem evidence has been disposed of in the discussion of the pathology of the shoulder injury, and I would again refer particularly to the quotation from Ashhurst, with which I fully agree.

²⁹ Deutsch. med. Wehnschr., 1914, xl, 1053.

³⁰ Ztschr. f. Orthop. Chir., 1914, xxxiv, 511.

³¹ Berl. klin. Wehnschr., 1914, li, 1162.

³² Jour. de Brux., 1912, xvii, 117.

³³ Internat. Clinics, vol. iii, series 26.

The experimental work has played a great part in supporting the Duchenne-Erb view. Fieux,³⁴ by lateral bending of the neck in the cadaver produced tearing of the roots of the brachial plexus most marked in those arising highest in the neck. He also produced a paralysis of the upper extremity in a rabbit by lateral bending of the neck. Shoemaker, after exposing the brachial plexus, like Fieux, in the cadaver of a newborn, prepared by alcohol, could not produce a tear of the plexus, but accepted the results and conclusions of Fieux for most of his cases. Taylor³⁵ made twenty dissections on ten infants within three to ten days after death. He found that tension was the only factor concerned in the production of the plexus lesion responsible for Erb's paralysis. By tension he produced a rupture at or about the junction of the fifth and sixth cervical roots of the plexus, in the twenty plexuses, *i. e.*, on both sides of the ten infants. He says "great force must be employed to cause the lesion." Sever's experiments consisted in applying traction and forcible separation of the head and shoulder in "numerous dissections on infantile cadavers." It is a little difficult to determine the results of the force applied, but one obtains the impression from his statements that with forcible separation of the head and shoulders, without lateral bending of the neck, the cords of the plexus could not be ruptured, but were made to "undergo dangerous tension and stand out like violin strings." He goes on to say that: "With the shoulder held and the head carried to one side, with the clavicle intact, considerable force was necessary to injure the plexus," and that "Even with considerable force the fifth and sixth nerves could not be completely torn across at Erb's point but frayed out inside the sheath, which always gave way first." With the clavicle removed it was easier to injure the plexus, but the clavicle is practically never broken in these cases, so that this experiment does not concern the problem at hand.

It is evident from the preceding experiments that much force is necessary for the production of a tear of the plexus by traction in the cadaver. In looking for a similar force during the delivery of a child we must keep in mind that forceps traction cannot be exerted on the brachial plexus because such traction can occur only after the head is delivered when the forceps are put aside. In most deliveries when the head is out the shoulders soon follow without much traction, often without any. Indeed, one will have no difficulty in finding cases in the literature of obstetrical paralysis developing after spontaneous birth. A case of this kind, reported by Roulland, has been mentioned on a preceding page. Labor was normal in 32 of the 471 cases reported by Thomas and

³⁴ Ann. de Gynee., xlvii, 52.

³⁵ AM. JOUR. MED. SC., October, 1905, p. 675.

Sever. In view of the results of the above experiments, particularly those of recent years, it is hardly conceivable that the mild lateral bending of the neck necessary for the delivery of an occasional obstructed shoulder will be sufficient to tear the brachial plexus.

I have tried the effect of direct extension on the head and lateral bending of the neck in six bodies of newborn infants, for which the following manipulations and results will be sufficiently representative to answer for all. Placing the body face downward approximately in the L O A position I applied the ordinary forceps (obstetrical) to the head, and while an assistant made counterextension on the shoulders, with my feet braced on the floor I pulled as hard as I could on the forceps—harder, I believe, than any competent physician ever pulled in a successful delivery. This was repeated two or three times. Then placing the right side of the neck on a suitable block of wood, with one hand on the head and the other on the shoulder, I bent the neck over the block with all of my force. This maneuver was repeated twice, after resting between the efforts. I then went through the same procedures on the opposite side of the neck. Dissection of the plexus on both sides showed no visible rupture at any point in either plexus. With the plexuses dissected clean of all traces of their sheaths the direct traction and the lateral bending on both sides were repeated with the same force as before while watching the plexus of each side in turn for any evidence of rupture, but none was detected. It may be well to bear in mind that as the traction is being applied to the neck and plexuses the continuations of the plexuses, the nerves, are surrounded by loose connective tissue and offer little resistance to the traction. If the dead nerves withstand such traction live ones are more likely to do so.

TREATMENT. The length of the preceding discussion concerning the etiology is worth while only if it leads to a more simple and effective method of treatment. Efficiency is the order of the day and obsolete ideas and methods are being ruthlessly set aside. One will have difficulty in showing any real progress in the treatment of these cases based upon the pathology of a plexus rupture. Lange spoke of it as the "let alone treatment." The rapidity with which the shoulder-joint treatment has been taken up by the profession since it was based upon a shoulder-joint origin of the condition, indicates that the theory of a brachial plexus origin is being rapidly set aside as surely as the same theory for the adult cases has long been obsolete. While practically all surgeons interested in the condition have adopted the shoulder-joint treatment the acceptance of the shoulder-joint origin has not been so general. Platt, perhaps, best expresses the mental attitude of most surgeons when he says: "As the treatment (of shoulder) is the same for all, the diagnostic disability (as to the seat of the causal lesion) is happily not of great

importance." As an indication of the rapidity and completeness with which the shoulder treatment is being recognized this is very satisfactory. But it is not enough because it is not all that the theory of a shoulder-joint origin offers. The shoulder-joint is injured at birth or it is not. If it is injured at birth that is the time to correct the damage, not many years afterward, nor many months or days. If there is no displacement in the joint, complete recovery will probably follow sooner or later, without special treatment; but if there is a displacement, and this is permitted to "heal in" for a few weeks, the chances are that nothing short of operation will restore the joint to the normal. If the correction is delayed a year the chances are that the normal joint relation cannot be restored even by operation. Sever says that the mere division of the sub-scapularis tendon is followed by the reduction of the dislocation. Much depends upon what we consider reduction. I have made persistent efforts at reduction in my earlier cases but with little success so far as actual change in the relations of the humerus and acromion are concerned. I am inclined to agree with G. G. Davis, that the good results of the operation are "due not to replacement of the head of the humerus but to the free division of restraining tissues and the placing of the parts in a better position."

We shall not obtain the best results, in my opinion, until we appreciate what went wrong at birth and make our efforts to correct it then. The only way in which this can be demonstrated is by the results in cases so treated. It is probably impossible to determine exactly what happens to the shoulder, but I believe one can obtain a crude but still effective conception of the mechanism of the shoulder injury from a close study of the typical deformity itself. In my judgment only one conceivable cause can account for this deformity, and this will account for every feature of it. The part of the child most liable to damage as it comes through the bony maternal pelvic ring is the widest part, at the shoulders. In rare instances Nature has not provided enough room, and one shoulder, probably the anterior, is jammed out of shape as it is passing under the pubic arch, temporarily or permanently according to the degree of compression. In either case there is a severe brachial paralysis from involvement of the axillary nerves in the consequent axillary inflammation, and the shoulder-joint soon becomes stiffened from the resulting cicatricial contraction. But the inflammation subsides and the cicatricial tissue is absorbed, so that the paralysis gradually disappears, the permanent crippling being due to permanent injury to the shoulder-joint. The elbow suffers often in less degree, but this phase of the subject is left out of the discussion now because it confuses the more important phase.

The shoulder deformity has always been the same in my cases except as to degree. It has three very important characteristics:

internal rotation of the humeral head and therefore of the whole limb, mild posterior displacement of the humeral head and bending downward over the head of the acromion antero-externally. The internal rotation is obvious, but the other two characteristics have not received attention until recent years because of their obscurity. They will probably continue to be overlooked in many cases. It may be almost impossible soon after birth to decide the question. There is one pathognomonic sign of the subluxation: On the normal side the upper end of the humerus projects a variable distance in front of the anterior edge of the acromion. On the side of the subluxation it cannot be felt from in front and by careful palpation with the finger the anterior edge of the acromion can be located a considerable distance below its normal level. On the normal side there is a hollow under the posterior border of the acromion; on the affected side, a prominence. The same pressure which forced the head backward bent the acromion down in front of it. It is this bent acromion in front of the humeral head that accounts for the permanency of such a mild subluxation, *i. e.*, permits the head to rest on the posterior glenoid margin without slipping back into the glenoid cavity. It is likely that the cases of obstetrical paralysis without subluxation are those in which the head was not pushed backward enough to allow the acromion to be bent down in front of it. The lesion common to both is the injury to other joint structures, particularly the capsular ligament. I have never seen a permanent palsy or crippling of the limb without a subluxation of the shoulder-joint, except in one in which there was some ankylosis and deformity of the elbow, and in that one the functional disturbance was very slight.

The only treatment that I have followed has been to restore the shoulder-joint to as near the normal as possible. Most physicians know something about the difficulties associated with old unreduced dislocations of the shoulder-joint in adults, so that it will not be necessary to emphasize the difficulty of restoring the shoulder-joint to the normal in these children in the presence of a long-standing subluxation, with the acromion and humeral head deformed by the original pressure and by later abnormal growth.

We are only beginning to appreciate the importance of this phase of the subject. To repair the damaged shoulder to the best effect is a large problem. My chief ambition is to be permitted to treat a case with dislocation within a day or two after birth. I have had such a case three weeks after birth, but that was too late for my purpose, as the cicatricial or healing process had been practically completed and reduction of the displacement by non-operative methods was impossible. I have seen two cases five days after birth, but there was no dislocation in either. One had a mild grade of paralysis which completely disappeared in a

few months. The other had a severe grade of paralysis, but this has been slowly disappearing, fast enough to satisfy the parents, and I still have it under observation. In all probability no case with a dislocation of the shoulder has ever recovered a normal arm, although with shoulder treatment they have been very much improved. According to my experience the improvement is largely in proportion to the degree of improvement obtained in the shoulder-joint. Manifestly the best time to correct the deformity there is when the displacement is recent, *i. e.*, at or very soon after birth. How to obtain the best results at this time is still an unexplored field.

CONCLUSIONS. 1. Obstetrical or brachial birth palsy represents only one phase of a much larger shoulder-joint problem. Almost if not all shoulder-joint injuries are associated with a brachial paralysis, palsy or weakness of varying degree and duration. Very rarely will an actual nerve rupture be associated with the paralysis.

2. The best evidence of the absence of such a nerve rupture is the almost uniform and gradual disappearance of the paralysis. This is easily proved in connection with the adult cases, and seems to be true of the obstetrical cases, in which the paralysis is usually of longer duration and more difficult to follow up. If the crippling of the limb persists into adult life it will probably be found in all cases that a posterior dislocation of the shoulder is associated, often with some moderate permanent disturbance in the elbow-joint.

3. In obstetrical paralysis soon after birth there is a profound and almost if not complete paralysis of the whole limb and not a paralysis limited to the small Duchenne-Erb group of muscles. This extensive paralysis is best explained by the inclusion of the branches of the brachial plexus in an axillary inflammation consequent upon a birth injury of the shoulder-joint.

5. The extravasation into the axilla of blood and synovial fluid causes an immediate inflammation and later cicatricial tissue, all of which is probably absorbed in time, thus accounting for the disappearance of the paralysis. Such a pathology has been well established by operative and postmortem findings in the obstetrical and adult cases.

6. The Duchenne-Erb localization of the paralysis by electrical reactions to the deltoid, biceps, brachialis anticus (Duchenne and Erb), infraspinatus (Duchenne) and supinators of the forearm (Erb) has been widely accepted but not corroborated.

7. In his first four cases Duchenne found posterior dislocation of the shoulder which he said occurred at birth and was chiefly responsible for the paralysis. He thought, however, that some of the paralysis was due to injury of the brachial plexus. In four later cases he did not find dislocation of the shoulder in any and attributed the paralysis entirely to injury of the brachial plexus. Since then practically nothing has been said of a shoulder-joint origin, the

dislocations passing unrecognized, and all cases being attributed to injury of the brachial plexus. Since 1911, when the shoulder-joint injury was offered as the primary cause, this theory has made rapid progress.

8. It is very likely that sufficient traction on the head at birth to rupture the brachial plexus has never been applied in a successful delivery.

SIXTH NERVE PARALYSIS OF OTITIC ORIGIN: GRADINEGO'S SYNDROME.¹

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DURING the years of 1916 and 1917 I have had the opportunity of observing 2 cases illustrating this unusual complication of otitis. In the first case the appearance of the ocular paralysis caused considerable apprehension, as I was unfamiliar at the time with the type of case so fully described by Gradinego. The second case, coming a year later, after I had had an opportunity of familiarizing myself with Gradinego's paper, was very interesting, but did not cause the same anxiety on account of the favorable course which he has found usual in these cases. In presenting the two cases I have taken the opportunity of giving a synopsis of the original paper, which I feel will be of interest to any of the members who are not already familiar with it.

In 1904 Gradinego reported² a series of cases in which the three cardinal symptoms, suppurative otitis, severe pain referred to the side of the head, and paralysis of the sixth nerve, were present in combination. There were 5 cases of his own and others collected from literature.

The publication of his paper caused considerable discussion, and there was some doubt expressed as to whether the sixth nerve paralysis was really a complication of the otitis or a coincident symptom from some associated condition, such as suppuration of the sphenoid or an independent cranial nerve palsy.

In 1907 Gradinego³ published a further paper on the subject and collected a series of 57 cases which illustrated his syndrome and established it as a definite clinical type. This syndrome he explains by the hypothesis of a localized meningitis from extension of the middle-ear suppuration through atypical pneumatic cells connected with the region of the Eustachian tube and extending more or less completely to the tip of the pyramid. These cells have been

¹ Presented at the Canadian Medical Association Meeting, Quebec, P. Q., June 26, 1919.

² Arch. f. Ohren., 1904.

³ Ibid., 1907, vol. lxxiv.

described by various authors, but perhaps most beautifully demonstrated by Siebenmann, of Basel, by his corrosion method.⁴

Gradinigo's work is of great interest as explaining the somewhat unusual complication of sixth nerve involvement by otitis and also as indicating a group of cases which, if neglected, may go on to a diffuse meningitis and death.

Reviewing the 57 cases he was able to classify them into three groups:

In the first group were 24 cases which showed a classical syndrome without other complicating features, beyond perhaps more or less inflammation of the mastoid. These cases ran a favorable course to complete healing and recovery.

In the second group there were 29 cases showing a typical syndrome but complicated by other lesions, such as seventh nerve paralysis, labyrinth irritation or optic neuritis, which he regarded as independent complications of the otitis rather than characteristic of the lesion by which he explains his syndrome.

In the third group were 4 cases which, in addition to showing the syndrome, later developed septic meningitis and died. He regards these as a more virulent type in which the process extends to diffuse meningitis; the second group illustrates an intermediate stage between the first and third.

The characteristic features of the syndrome are mentioned in detail:

ACUTE SUPPURATIVE OTITIS. Usually the otitis in these cases is characterized by evidence of retention of pus in the middle ear, either complete or relative. This is indicated by absence of or insufficient perforation of the drum. In 32 cases in which details are given eighteen times there is no perforation, or there was late spontaneous perforation, or paracentesis was done late. The perforation was generally too small, so that it required subsequent paracentesis. Sometimes this was repeated as many as five times. It was also striking that the situation was frequently in the anterior half of the drum. Paracentesis, or enlargement of the perforation, was generally followed by a striking remission of the symptoms, pain and paralysis thus showing a definite relationship between the otitis and the paralysis of the sixth nerve. This remission of the paralysis after middle-ear drainage was well shown in my first case.

SEVERE PAIN. Severe pain was referred to the temporal and parietal regions of the side involved. The otitis is characteristically accompanied by very severe pain, which, however, may subside a few days after the appearance of the discharge. This is referred to the deeper parts of the ear, or more characteristically, to the side of the head, occasionally to the retroorbital region. It is not characteristic of a fifth nerve neuralgia, which is paroxysmal, but is

⁴ *Anatomy of the Middle Ear, etc., Bardeleben's Handbook.*

more intense and continuous and is little relieved by antineuralgic remedies. It sometimes appears two or three weeks after the discharge at the time of the appearance of the paralysis.

PARALYSIS OF THE SIXTH NERVE. This symptom appears suddenly without warning, the patient sometimes complaining of a diplopia, and calls the attention of the physician to it. Paralysis does not usually appear early. In the 37 cases in which the exact appearance was noted: Three times it appeared early on the fifth to the tenth day; eight times it appeared from the fifteenth to the twentieth day; twenty times it appeared from the twentieth to the fiftieth day. Occasionally it is late; in 6 cases it was after the fifty-sixth day. It may be stated, in general terms, as occurring from three to six weeks after the beginning of the otitis. In the typical cases complete recovery usually occurs, but is liable to be slow. There are unusual cases in which the paralysis disappears rapidly, and to this type both of my cases belong.

The complicating symptoms of the second group were suggestive of a meningeal irritation.

COMPLICATIONS IN THE MASTOID. Complications in the mastoid were regarded as associated with a severe otitis, but having no direct bearing on the syndrome. In the 57 cases there were only 24 in which a mastoid operation was done; usually it was for the purpose of free drainage of the middle ear rather than for the relief of symptoms pointing to a mastoid involvement. The findings in the mastoid at operation were usually an inflamed mastoid without severe local disease, although in some cases there was mastoid abscess or even a perisinus abscess.

The seventh nerve paralysis, when present, was regarded as an independent manifestation, probably from involvement of the nerve in the region of the middle ear.

Certain features, such as the late appearance of the paralysis, are explained by the disease lying latent in the pneumatic cells of the pyramid, just as we often find foci remaining latent in the pneumatic cells of the mastoid and later setting up active trouble.

Other theories which have been advanced to explain the sixth nerve paralysis are found untenable.

It has been suggested that on account of the relations of the labyrinth to the ocular muscles it might arise in some way by labyrinth involvement. Characteristically, however, there is no involvement of the labyrinth in these cases.

It has also been suggested that we might have here an associated neuritis of the sixth nerve. The condition, however, occurs too constantly as part of the syndrome and the relation with the otitis is too definite for such an explanation.

In 2 cases there was a history of syphilis or a positive Wassermann reaction, but even in these the paralysis was quite uninfluenced by

antisyphilitic treatment, and the syphilis was regarded as an accidental finding, with no direct bearing on the symptoms.

The history of my own cases was as follows:

CASE 1.—J. R., male, aged twenty-two years, consulted me on May 1, 1916, complaining of profuse discharge from the left ear.

Onset of Illness. Illness began two weeks ago, with very severe earache and headache, followed a few days later by discharge. The pain, however, was not relieved by the discharge and two days ago it was again very severe and accompanied by considerable fever.

Present Condition. On the examination the patient is a poorly nourished individual and looks ill, but shows no elevation of temperature. The left ear shows profuse mucopurulent discharge, which is pulsating. The drum membrane is injected and shows a perforation in the lower anterior part of fairly large size, suggesting chronic perforation. There is a slight fulness of the upper part of the drum and some slight swelling in the wall of the canal; there is no pain or mastoid tenderness.

The case was put on conservative treatment, frequent syringing with hot boric lotion, and for ten days there were no unusual symptoms. It must be stated, however, that the patient was of a rather sluggish mental type, and it is possible that pain might have been present without his complaining about it.

On May 10, about three weeks after the onset of the otitis, it was noted there was a paresis of the left external rectus. I referred the patient to Dr. McAnley for a report on the eyes, and his report stated that beyond a paresis of the left external rectus there was nothing abnormal to be made out. The fundus was normal.

The following day there seemed to be some increase in swelling in the canal and I decided to drain the mastoid. The outer table was very thick, the cells of the mastoid were small, filled with pus, but no marked destructive process in the bone. Following the operation there was a persistence of discharge from the canal, suggesting that the mastoid drainage had not been sufficient to relieve the supuration of the middle ear. The condition improved for a day or so and the paralysis was less marked, but on May 23, probably from the obstruction of the aditus by granulations, the paresis became decidedly more marked and there was a slight elevation in temperature. As the right ear was normal I decided to perform a radical mastoid operation to ensure the complete drainage of the whole tympanum. This was done on May 25. The middle ear was full of pus and swollen folds of mucous membrane.

On May 27, two days after operation, there was a very striking improvement in the paresis, which gradually disappeared, and on June 9 it was reported absent. The ear healed rather slowly, but on July 3 he was discharged healed, though there was still some slight mucous discharge from the region of the Eustachian tube.

The case belongs, I think, to the first group described by Gradinego

and illustrates a favorable outcome to what looked at the time to be a case going on to an intracranial complication.

CASE II.—M. O., female, aged twenty-eight years, was seen on April 30, 1917. The history was that her right ear had been sore for five weeks and had been discharging since April 5, a little over three weeks. Pain at onset had been severe for over two weeks, when a paracentesis had been done, with a certain amount of relief. For the past two or three days the discharge had been profuse and the pain had reappeared.

On examination her general condition was somewhat below par, her temperature being 100°. The right ear showed a somewhat congested drum, with a bulging nipple-like perforation, indicating retention. On the following day she was operated on, a simple mastoid operation being carried out. The cells were filled with swollen mucosa, but there were no marked changes in the bone. A free paracentesis was carried out at the same time, and there was evidence of a certain amount of retention in the middle ear. The wound healed rapidly and the discharge from the ear stopped a day or so after the operation.

On the third or fourth day after operation (about six weeks from the onset of the otitis) she developed a paresis of the right external rectus, but as the ear condition gave every evidence of satisfactory healing, no further interference was carried out, and the paresis disappeared spontaneously in three or four days.

This last case is interesting as illustrating the development of the paresis after the middle-ear condition was on the high road to recovery.

A CLINICAL PATHOLOGICAL STUDY OF AN UNUSUAL SYPHILITIC MANIFESTATION RESEMBLING JUXTA-ARTICULAR NODULES.

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THE case which forms the material for the present study was seen more than a year ago, but the exigencies of the period delayed this report.

At the time this case was first seen an effort was made to find reference to a like condition in the available literature. Although mention of syphilis of the tendons was frequent enough, no study was found which compared with this case. We were led to believe

that we were dealing with a rare syphilitic manifestation which merited reporting.

CASE REPORT. The patient, R. R., was an American woman, aged twenty-nine years, and of more than average intelligence. She was born in New York and had never left the country. Her father had died of tetanus at forty-nine years; her mother of an unknown cause at forty-six years. The patient had three brothers and sisters alive and well. There had been one stillbirth among her mother's pregnancies, and one child which had weighed three pounds at birth died at thirteen days.

R. R. had married at eighteen years. She had one abortion at four months and did not become pregnant again. Her husband, who had always been well, died in a railroad accident, after two years of matrimony.

At twenty-two the patient married again. Although her husband is healthy, and they desire children, she has not become pregnant.

Except for a vaginal discharge after the abortion the patient had never been sick. She is certain that she has never had a disease of the skin or mucous membrane.

The presence of tumors on the extremities had been noted for about eight years. The first lesion was on the extensor surface of the left elbow and about the size of a pea. Additional masses have appeared since in an unnoted order, and usually were noticed accidentally. For instance, the mass on the knee was of appreciable size when first noticed four years ago. Until her present consultation the patient had never shown these lumps to a doctor and had not taken treatment.

Physical Examination. Patient is an adult white woman weighing 178 pounds. The hair of the head is profuse and well distributed. The shape of the head is normal. There is no mastoid tenderness nor discharge from the ears. The external ear presents no irregularities. The eyes are hypermetropic and require lenses. The pupils are central, equal and react to light and accommodation. The nose is negative. The tongue presents a superficial but non-fissured glossitis. The tonsils are enlarged and are slightly erythematous. The palate is highly arched, but with no suggestion of perforation. The teeth are all present and well preserved. There is no notching of the incisors.

The thyroid is not enlarged. There are no pulsations visible in the neck.

The lungs are resonant throughout.

The woman is rather fleshy and large mammae overhang the area of heart dulness, so that the left border is rather difficult to determine. There is no enlargement to the right. There is no bulge over any part of the anterior chest wall. No cardiac impulses are seen. The heart rate is 82. The sounds are normal. The rate at the radial pulse is the same as the heart and of good quality.

There is no suggestion of the "water hammer" of Corrigan. The blood-pressure was not determined.

The smooth liver edge was felt under the costal arch. There were no masses felt in the abdomen. There was no tenderness elicited by pressure anywhere over the abdomen.

The skin and mucous membranes were free of any lesions or scars.

The patient was menstruating and no vaginal examination was made.

The contours of the extremities were normal, except for nodules at both elbows and over the left knee.

The nodules on the left elbow extend in a line from the olecranon process to the styloid process of the ulna. The first is situated two inches from the olecranon. It is semiglobular and about 3 by 2 cm. It lies entirely under the skin, which is freely movable over it. The tumor appears attached to or part of some subcutaneous structure, which limits motion of the mass except for about 1 cm. in any direction. To the touch the mass appears lobulated and made up of individual although connected masses. These are distinctly hard and cannot be indented by pressure over them. The skin over the lesion is not stretched nor is it red.

The second tumor on the left arm is about 2½ cm. distant from the first. It is 3 by 4 cm. It appears made up of only two connected lobules rather than many, and otherwise is of the same appearance.

No other masses are present on the left arm.

The lesions on the right arm are symmetrically arranged with those on the left. The masses are of the same character as those of the left arm.

Over the left knee and in the ligamentum patellæ, occupying the space of the normal indentation between the patella and the tubercle of the tibia, is a single mass about 2 by 2 cm., which gives the same resistance and is of the same structure as that described for the elbow tumor. The mass moved with the motion of the leg upon the thigh and gives no discomfort. There are no other lesions present on the legs.

The clinical diagnosis of multiple gummata of the tendons was ventured by both Dr. Young and myself. Blood for a Wassermann was taken and part of one of the nodules removed for section. The incision healed nicely.

The Wassermann was reported four plus positive to both alcoholic and cholesterinized antigens. (Laboratory of the New York Skin and Cancer Hospital.)

Radiographs taken by Dr. Young showed the nodules as outline of soft parts. No shadow of bone nor connection with bone was found.

The biopsy material was sectioned and stained.

Preparations with Levaditi silver impregnation were made and prolonged search for *S. pallida* proved unavailing.

Microscopically the tissue of the tendon was interspersed with larger and smaller accumulations of round cells. These aggregations were about the bloodvessels, which were unusually numerous and indicated that new bloodvessels and capillaries had formed in tendon, which is ordinarily almost free of bloodvessels. The type of cell predominating in the peri-arterial gummata was the round cell with occasional spindle-shaped epithelial cells. There were no giant cells nor polynuclears. There was no evidence of caseation nor necrosis. No cartilage nor bone had formed.

The bloodvessels were extremely numerous for tendon. The majority were of the single layer capillary form. The lumen of even the smallest was open and the lining appeared uninjured. No vessel was seen of sufficient size to show evidence of the infiltration of the coats.

There was no formation of a fibrous connective-tissue wall about the mass. It was apparently a diffuse process. The histopathological diagnosis was "granuloma, probably syphilitic."

We have considered that the patient received her syphilitic infection at the time of her first marriage. The early abortion and the subsequent barren period of eleven years is evidence in favor of this. The first appearance of this unusual lesion occurred three years after the syphilitic infection. Speculation as to the localization of the spirochetes, to which the gummatus process is the reaction, would be confined to the theory that in the period of spirochetemia, spirochetes lodged locally in the infrequent end-capillaries of normal tendon. The impetus for the reaction to the presence of the organisms may have been some mild injury to the exposed sites of the elbows and knees. The fact that the patient knows of no eruption nor sore that would indicate syphilitic infection does not exclude her syphilitic infection. That the nodules did not ulcerate we believe to be due to the low plane of the metabolism of tendon.

At the time of the clinical examination the differential diagnosis presented little difficulty. Bursitis, ganglion, tophi, tendosynovitis and sesamoid bones were all easily overruled.

Recently the attention of one of us (G) has been drawn to the clinical resemblance between this described gumma lesion and juxta-articular nodules.

Juxta-articular nodules were first described by Jeanselme in 1899 among the Indo-Chinese. (To translate): "Clinically the nodules are of various sizes, globular or polyglobular, most often collected in masses. In the beginning the tumors lie deep in the subcutaneous tissue. Some of them are movable and roll under the fingers like ganglion; others appear adherent to the periosteum, from which they possibly originate. Later, these nodules become more superficial and are incorporated in the skin. Later still they raise from the surface as protuberances of very hard consistency. The skin undergoes no modification; it is only distended and perhaps dis-

colored at the highest point. The nodules are remarkably symmetrical. They occupy the external aspect of the extremities, surmounting by preference the bony prominences and grouping about joints. The points of predilection on the lower extremity are: the external malleolus; head of the tibia; tubercle of the tibia; anterior surface of the knee; trochanteric and sacrococcygic regions; on the upper extremity: the olecranon; epitrochlear; acromium; and dorsal surface of the digits."

The generally ascribed cause for the nodules is the result of the habit of the natives to lie with the elbows and knees in contact with the ground.

"On section studied with low magnification the nodules are divisible into three zones—an internal or zone of degeneration, an external or inflammatory and an intermediate or zone of transition.

"The degenerative zone is formed of irregular blocks, homogeneous and translucent, which stain a deep red with eosin. These blocks are fissured in all planes and their contours are convoluted. With higher magnification (ocul. I, obj. 6) the degenerative substance is subdivided into two portions; the first, really homogeneous, is a clear red; the second portion is more or less merged with the preceding and is vascular, slightly fibrillar and a violet red. In the spaces which separate the blocks into fragments are various ordinary polynuclears undergoing disintegration. The number of these leukocytes increases as one approaches the periphery of the degenerated mass. The leukocytes are situated in the large otherwise empty spaces which appear cut out by a punch in the dense fibrous tissue. At the borders of the large empty spaces are disseminated some smaller degenerative blocks, all easy to recognize, even the smallest, by the bright red color.

"The zone of inflammatory reaction is made up of two very different structures: one of fibrous tissue, the other of yellow meat like tissue. In the latter one finds: large and anastomosing fixed cells within a reticulum where the network is filled by criss-crossing fibrils in all planes; some fixed cells, freed in the form of macrophytes; some giant cells, with nuclei originating from connective tissue; innumerable plasma cells in the interstitial spaces; considerable number of polynuclears, most of the ordinary type, and some eosinophiles; and finally numerous blood and lymph capillaries, which consist of only one layer of flattened or raised epithelial cells.

"Between the frank inflammatory zone and that of sclerosis there exists some transitional forms. Little by little the collagen elements predominate over the cellular, the fibrils dispose themselves in thick bundles, separated by proper interstices, forming a mosaic of fixed flattened cells. Little by little the vessels become fewer and their walls thinner, and a compensatory diminution of the polynuclears exists.

"The zone of transition between that of degeneration and that of

inflammatory reaction is characterized by a gradual homogenization of the connective tissue which loses the fibrillar condition and stains deeply with eosin. Between the focus of necrosis and focus of the inflammatory area begins an eliminating sulcus which gradually causes the degenerative tissue to form as a foreign body within the fully sclerosed tissue.

"The bacteriological examination has been completely negative. In sections stained by Ziehl or Gram, or after treatment with 40 per cent. potassium hydroxide, we have never demonstrated any microbes.

"The microscopic examination has revealed nothing as to the nature of the nodule. They certainly do not reveal syphilis nor tuberculosis, nor any suggestion of xanthoma which have characteristic structures. The possibility of tophi naturally presents itself, but the site of the small tumors, their multiplicity, indolence, structure, absence of tophi of the ears, the rarity of pains and malformations about the joints, and finally the regimen of the class of poor affected are little in favor of such a supposition. The nodules are not fibroma, nor sclerosed forms of peri-articular bursa."

It has been thought wise to give a rather full account from Jeanselme on juxta-articular nodules because of the scant attention paid to them in most of the English works, even those on tropical medicine. Were it not for the histology we believe it would have been difficult to differentiate the case of multiple gummata of the tendons from juxta-articular nodules.

SUMMARY. A case of multiple and symmetrical gummata of the tendons is described which clinically closely resembles the tumors of juxta-articular nodules. The microscopic picture is very different, however, and hence the two conditions cannot be confused.

Unfortunately we were not able to observe the effect of anti-syphilitic treatment, but the suggestive history, positive Wassermann, and histology of one of the lesions puts the diagnosis of multiple syphilitic gummata of the tendons on a sound basis.

Thanks are extended to Dr. Elizabeth Finch for her aid in the technical study, and to the director of the Institute of Tropical Medicine and Hygiene, San Juan, Porto Rico.

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CONGENITAL ABSENCE OF ONE LUNG.

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CONGENITAL absence of one lung is a rare condition. Twenty-one cases are reported in the literature. They are, briefly, as follows:

1. *Haberlein*:¹ Soldier, aged twenty years, who had respiratory difficulty. Absence of left lung. Left thoracic cavity filled with fluid. No left bronchus. Heart in normal position.

2. *Haberlein*:¹ Right lung absent in a soldier, aged twenty-four years. Left lung abnormally large. Right thoracic cavity filled with fluid. Both primary bronchi and all pulmonary vessels entered left lung.

3. *Bell*:² Young man, aged twenty-four years, a Pole, in the German service, who had had some respiratory difficulty since birth, died suddenly sitting up in bed. Right lung absent. Both primary bronchi entered the left lung. No right pulmonary vessels.

4. *Bell*:² Absence of left lung in young man; absence of left bronchus and left pulmonary vessels. Heart on the right side. Aorta small.

5. *Hein*:³ Six weeks' old male child, very cyanotic. Right lung absent. Rudimentary right bronchus. No right pulmonary artery or veins. Ductus botalli wide open. Foramen ovale patent.

6. *Maschka*:⁴ Premature child who lived two hours. Right thoracic cavity completely filled with pericardial sac and contents. Right lung absent. Right bronchus a pea-sized, closed pouch. Left lung single lobed. Absence of right pulmonary vessels. Esophagus ended blindly at about its middle point, but below communicated with the trachea.

7. *Stein*:⁵ Six weeks' old child. Right lung missing. Rudimentary right bronchus. No right pulmonary vessels.

8. *Grüber*:⁶ Stillborn child. Absence of right lung and right primary bronchus.

9. *Herrero*:⁷ Man, between sixty-five and seventy years, found dead on the street. Left lung absent. No left primary bronchus. Right lung hypertrophied.

10. *Theremin*:⁸ Girl, one hundred and twenty-seven days old. During life moist rales were heard in upper part of left chest and signs of pneumonia on the right side. Normal conformation of chest. At autopsy the left lung was found to be absent. Left thoracic cavity filled by pericardial sac; pericardium adherent to walls of thorax. Left primary bronchus represented as a pea-sized pouch.

No left pulmonary vessels. Left auricle received no vessels, but a single pulmonary vein emptied into the vena azygos.

11. *Theremin*:⁸ Girl, eleven days old, died of pneumonia. During life, bronchial breathing on both sides posteriorly. No deformity of chest. At autopsy, left lung absent. Hemispherical cartilaginous pouch of left bronchus. No pulmonary veins entered the left auricle, but these united to form a large vessel which communicated with the vena azygos.

12. *Grüber*:⁹ Premature child, born dead. Left lung absent. Chest symmetrical. Three short branches of the trachea at the hilus of the right lung. Left thoracic cavity filled with pericardial sac. Pulmonary artery divided into a right pulmonary artery and the ductus arteriosus.

13. *Tichomirow*:¹⁰ Girl, aged twenty-four years. Chest symmetrical. Absence of left lung and left primary bronchus. Three branches of right primary bronchus. One right pulmonary vein.

14. *Findlayson*:¹¹ Child, who lived few hours after birth. Right lung absent. Trachea ended in left bronchus. Left lung hypertrophied.

15. *Gross*:¹² Child, five months and twenty-three days old. Atresia ani. Asymmetry of face. Left lung absent. Right lung filled the right thoracic cavity and the small part of the left. Left primary bronchus ended 1 cm. long. Heart hypertrophied and filling left thoracic cavity. Right lung emphysematous. Left pulmonary vessels absent.

16. *Ellis*:¹³ Boy, aged eight years, with diagnosis of acute articular rheumatism and acute endocarditis. Chest symmetrical. Physical examination: Expansion good but diminished on left. Dulness posteriorly to midaxillary line. Tubular breathing as far as midline on this side. Roentgen-ray diagnosis: effusion of left side of chest. Autopsy: Left lung absent. Right lung well beyond the costochondral line and twice the normal size. Large pericardial sac occupying remainder of left side of thorax. No left pulmonary artery or veins. Left bronchus 2.5 cm. long, ending as a blind pouch and covered with grayish tissue, which microscopically showed cellular-fibrous tissue, with ill-defined spaces lined by epithelium.

17. *Tebbutt*:¹⁴ Boy, aged twelve years. Heart 15 cm. to the left of the sternum. Left side of thorax dull posteriorly. Presystolic and systolic murmurs at apex of heart. Roentgen-ray report: heart enlarged and pushed over to the left. Autopsy: Left lung absent. Left side of thorax occupied by the heart. Distended pericardial sac and pericardial adhesions. Pulmonary artery divided into two branches before entering the right lung. Pulmonary vein formed by junction of two main vessels, which themselves were formed by two or three smaller veins soon after leaving the right lung. Endocarditis of the mitral and aortic valves.

There are, in addition to these reports, four cases in the literature

where a possible rudimentary lung has been found covering an imperfectly developed primary bronchus.

18. *Miller*:¹⁵ Male, aged four weeks. Left lung the size of a pea. Left primary bronchus small and capped by rudimentary lung.

19. *Miller*:¹⁵ Male, aged six weeks. Left lung the size of a cherry, hanging on narrow bronchus.

20. *Miller*:¹⁵ Female, two days old. Left lung a mass of tissue, 2 cm. long, attached to narrow bronchus.

21. *Hanson*:¹⁶ Female child who lived fifteen minutes. Heart on the right side. Right lung smaller than normal. Left lung rudimentary and looked "like a bunch of millet-seed, not larger than buckshot, the left bronchus being simply a cord one-twelfth inch in length." Diaphragm absent on the left. Left thoracic cavity occupied by part of the small and the large intestines and the appendix just beneath the clavicle.

The cases of Bill, Flischmann, Meckel, Rivière, Pozzi, Sömmerling, Heyfelder, quoted by Förster (*Missbildung*) and by Fürst in Gerhardt's *Handbuch* are regarded as doubtful cases of congenital absence of one lung and have not been included in the above list.

Through the courtesy of the Department of Urology the writer has been enabled to report an additional case of congenital absence of one lung in a patient who was treated on the service for the urinary incontinence of *tabes dorsalis*. This is the first case of congenital absence of one lung in almost 6000 autopsies performed in the pathological department of the Johns Hopkins Hospital.

Clinical History. October, 1917.

H. S., aged forty-nine years; married. Family history negative. History of occasional slight dyspnea.

Patient had a sore on the penis at the age of eighteen (1888), which was apparently not followed by any secondary manifestations of lues. In 1912, he noticed that he had some difficulty in walking, particularly when walking toward the light, when he seemed to think that the ground was coming up to meet him. For one and a half years there had been nocturnal incontinence and some diurnal frequency. Examination at this time showed a positive Romberg and absent knee-jerks. On cystoscopy 300 c.c. residual urine was obtained. The bladder showed considerable trabeculation and cellule formation. The trigone was atrophied and the internal sphincter sufficiently dilated to make the verumontanum easily visible with the observation lens of the cystoscope. The diagnosis of *tabes*, with vesical involvement, was made.

In December, 1918, the patient returned to the clinic. For seven months he had been confined to his bed as a result of ataxia. His urinary incontinence had gotten worse, with constant dribbling day and night. From March to July, 1918, the patient had been catheterizing himself at irregular intervals. On May 23 he developed a right-sided epididymitis which subsided on incision and

drainage. In July, 1918, he developed epididymitis of the opposite side. Two sinuses discharging pus followed incision and drainage. In January and February, 1918, the patient received three intravenous and three intraspinal treatments for his tabes. He was under the care of Dr. E. L. Zimmermann, who reported a positive Wassermann of both the blood and the spinal fluid. The patient was admitted this time to the ward, following an incision of an abscess of the left epididymis.

Physical Examination. Showed a poorly developed, emaciated, middle-aged man, with atrophy of the muscles of both the upper and lower extremities, who walked with a typical tabetic gait; the thenar and hypothenar eminences of the hands were atrophied. He wore a urinal for incontinence.

Neurological Examination. Cranial nerves were negative. Pupils were equal but reacted sluggishly to light. The knee-jerks were present. Finger-finger and heel-tibia tests revealed marked incoordination. Romberg was positive. Movements of the big toe were not appreciated by the patient, showing definite loss of muscle sense. No ankle-clonus was present. Touch sensation was normal everywhere, but the patient was unable to distinguish between blunt and sharp sensations with the head or the point of a pin.

Head and Neck. Examinations were negative. No general glandular enlargement was present.

Thorax. Anteriorly the chest was asymmetrical and long. Retraction was present at both apices and in the interspaces. The left side of the chest was flatter than the right. Movement of the entire chest was restricted. Percussion note everywhere was impaired and flat at the apices. From the apices down to the second rib expiration was prolonged and suggestive of tubular breathing; everywhere else the breath sounds were bronchovesicular in character.

Posteriorly. Same asymmetry of chest existed, with marked bulging on the right. The spine showed convexity to the right in the cervical and thoracic regions. Vocal fremitus was diminished on the left and the percussion note was impaired over the entire left side and flat toward the base. On the right there was some impairment to percussion from the apex down to the angle of the scapula, otherwise the percussion note was normal on the right, with good descent of the lung on deep inspiration. On auscultation the breath sounds were tubular in quality in the region of the second and third thoracic spines on the right. The tubular quality stopped abruptly at the fourth thoracic spine. Below this the breath sounds were bronchovesicular. The breath sounds of the left side were suppressed, almost tubular in quality to the angle of the scapula, but vesicular below. At the left base showers of rales were heard at the end of inspiration.

Heart. Owing to the impairment of the percussion note on the left the relative cardiac dullness could not be made out. A diffuse pulsation was seen in the nipple line from the third to the fifth left interspace. Heart sounds were clear but distant in the aortic area. A soft, systolic murmur was heard in the region of the apex, but not transmitted to the axilla.

Abdomen. Examination was negative.

Genitalia. The penis was edematous. A discharging sinus communicated with the left globus major. The entire left side of the scrotum was indurated with scar formation and another discharging sinus was present at the lower pole. The epididymes on both sides were enlarged and nodular. The testicles could not be felt as separate masses from the epididymes.

Rectal. Numerous external hemorrhoids were present in a cauliflower arrangement. The anal sphincter was markedly relaxed. The left lobe of the prostate was of almost stony hardness. The right lobe of the prostate was small, flat and not indurated. The patient was discharged four days later, with the sinus of the left epididymis still draining.

On January 28, 1919, the patient received a Kollmaun dilatation. This was immediately followed by an elevation in temperature to 105° F., accompanied by tachycardia, chills and profuse sweating. The patient was admitted at once to the ward.

The physical examination did not differ materially from that of his previous admission. The pupils were equal but reacted sluggishly to light. The knee-kicks were obtained, but with difficulty.

The thorax showed the asymmetrical character previously noted. There was a marked depression below the xiphoid and retraction at both apices. Vocal fremitus was diminished on the left. The percussion note was impaired at both apices while the breath sounds were bronchovesicular in type in front. On the left, posteriorly, vocal fremitus was absent and the percussion note was dull in character and flat at the base. On the right, posteriorly the percussion note seemed to be normal. Scattered over the entire chest in front and behind were numerous rales.

The maximum impulse of the heart was in the fifth interspace, almost in the axillary line. The left side of the scrotum was still indurated and a discharging sinus was present at the lower pole.

On admission the patient was in extreme shock. The temperature varied between 104° and 105° F. for the first two days. On the third day the temperature became subnormal and remained so until his death, six days later. While in the hospital the patient had marked rectal incontinence. He gradually grew weaker and had attacks of respiratory difficulty, accompanied by shortness of breath and rapid pulse. Two days before death signs of bronchopneumonia were found in both lungs. For four days before death the patient had complete anuria. The blood urea was 1.7 grams

per liter. The patient died on February 5, 1919. The actual causes of death were regarded to be bronchopneumonia and uremia.

No roentgen ray of the patient's chest had been taken during life.

Clinical Diagnosis. Tabes with urinary and rectal incontinence; chronic fibroid tuberculosis of the left lung; bilateral pyelonephritis, uremia; bronchopneumonia.

Autopsy Report. Anatomical Diagnosis. Syphilitic aortitis; fibrous orchitis, tabes dorsalis; abscess of left testis and seminal vesicle; pyelonephritis (bilateral); dilatation of colon; congenital absence of left lung, left bronchus, left pulmonary artery and left pulmonary veins; abnormal course of left innominate vein, lobular pneumonia, calcified lymph glands.



FIG. 1

The thorax was asymmetrical, the right half more prominent than the left. In the middle of the anterior part of the left scrotum there was a small fistula from which thick yellow pus exuded. The organs of the abdominal cavity were normal. On opening the thorax a very remarkable condition was found. The right lung was of tremendous

size, completely filling the right pleural cavity and extending medially over the front of the mediastinum and into the anterior part of the left hemithorax, so that the uppermost anterior margin of this lung came to lie at the left apical region, to which it adhered. From the left apical region the anterior margin of the right lung extended downward and lay about 10 cm. from the midline.

As may be seen from Fig. 1 the anterior portion of the thorax was occupied by a large part of the upper lobe and by the whole middle lobe. The right pleural space was empty and the pleural surface was smooth and glistening.



FIG. 2

The left lung was absent. The size and position of the right lung displaced the heart to the left and posteriorly into the position usually occupied by the lower part of the left lung. The lateral and posterior surfaces of the pericardium were adherent to the chest wall by firm connective tissue. No traces of visceral pleura were found. At the left apex there was a small portion of dark pigmented tissue, which was independent of any connection with the lungs or the heart.

On removing the organs of the neck, together with the heart and lung, the following remarkable condition was seen.

1. The trachea was large in diameter and descended down to the region of the bifurcation. At this point a large primary bronchus proceeded toward the right lung, where the usual ramification took place. The left primary bronchus was represented only as a small, blind pouch at the point of bifurcation. This condition may have represented an attempt toward the formation of a left bronchus at an early embryonic stage (Fig. 2, *a*).

2. The pulmonary artery arose from the left ventricle as usual, then passed under the arch of the aorta toward the right side and divided into three branches. Each of these entered the upper, middle and lower lobes of the right lung respectively. No left pulmonary artery.

3. The pulmonary veins were made up of: (*a*) Two branches which arose from the upper lobe and which united into one trunk. (*b*) One branch which arose from the middle lobe. (*c*) One branch which arose from the lower lobe. These three trunks emptied into the left auricle separately. No left pulmonary veins.

4. The superior vena cava emptied as usual into the right auricle, but received only one innominate vein. The left innominate vein emptied directly into the right auricle.

5. The right vagus and phrenic nerves had their normal relations. The left vagus descended normally. The left phrenic nerve coursed close to the chest wall, owing to the absence of the left lung.

Heart. The cavities were large and the muscles hypertrophied; heart valves smooth and glistening. The base of the aorta showed many sclerotic patches. This condition existed along the entire vessel.

Lung. The pleura was smooth but somewhat thickened. The upper lobe was large and consolidated posteriorly and laterally. The lower lobe was air-containing. The elastic structure of the lung appeared to be greatly increased. Over the left uppermost part of the middle lobe there was an area of atelectasis. Glands at the hilum were enlarged and some were caseous.

Spleen, Liver, Adrenals, Pancreas, Gastro-intestinal Tract. Normal.

Kidney. The left kidney weighed 160 gm. and was of firm consistency. The capsule stripped with difficulty, leaving a rough surface. The pelvis was distended by yellowish-white, thin, purulent material. Striations of the medulla were indistinct. The cortex was pale and granular. The ureter was of large calibre.

Right Kidney. Weighed 220 gm. Of the same gross appearance as the left kidney, but no fluid had accumulated in the pelvis.

Genitalia. Right testicle of firm consistency and the tubules did not pull out readily. Left testicle was represented by a cavity filled with pus. A large abscess was found in the left lateral lobe and a small abscess in the middle lobe of the prostate. The bladder showed nothing abnormal grossly.

Brain and Cord. The dorsal columns were gray and translucent. Brain showed nothing abnormal.

Microscopic Examinations. Right lung: Some alveoli were filled with a large number of polymorphonuclear cells and desquamated epithelial cells. Some contained red blood cells and large mononuclear wandering cells. Sections stained with Mallory's connective-tissue stain showed connective-tissue structure increased. Section through the small mass of tissue seen in the region of the left apex was formed of fat, connective tissue, bloodvessels and one small lymph node, in no way suggesting pulmonary tissue.

Aorta. Mononuclear infiltration around the bloodvessels of the adventitia. Some areas of necrosis of media.

Testes. Hyaline changes in many tubules. No signs of spermatogenesis. Tubules rigid and surrounded by thick walls.

Kidneys. Actual necrosis of the epithelial lining of some of the convoluted tubules. A few hyaline glomeruli. Some areas of mononuclear infiltration.

Cord. Section stained by Pal-Weigert method showed marked degeneration of the posterior columns. Section of liver, adrenals, intestines, pancreas and bladder were normal.

In these 22 cases absence of the left lung occurred fifteen times and of the right lung seven times, showing a definite predilection for this anomaly on the left side in the ratio of 2 to 1. No satisfactory anatomical explanation has been offered for this left-sided predominance, but interference with the blood supply in embryonic life is supposed to be in some way responsible for it.

Life is not incompatible with one lung. The period of life in 10 cases has varied from eight years in one to about seventy years in another, twelve dying before the age of one year. The analysis of these 10 cases as regards duration of life is as follows: 1 case of eight years, 1 case of eleven years, 1 case of twelve years, 1 case of twenty years, 3 cases of twenty-four years, 1 case of fifty years, 1 case of seventy years, 1 case of a young man.

Respiratory symptoms have not been common and the patients have often come to autopsy for other than pulmonary conditions.

There has been a tendency for the one lung to undergo compensatory hypertrophy and to occupy part of the opposite side of the thorax. Atrophy of the lung is reported in one case (Hanson's). The pulmonary vessels have shown abnormalities which are not constant for all cases. The primary bronchus corresponding to the missing lung has usually been rudimentary and has often ended as a blind pouch. The absent lung has most often been replaced by a large pericardial sac, sometimes by fluid, and in one case part of the small and large intestines was found occupying the left thoracic cavity.

In the cases previously reported the chest has been described as normal in contour. The thorax in the case reported here was definitely asymmetrical, the left side of the chest being flat and the

opposite side bulging, this asymmetry was more marked posteriorly. Chiladiti,¹⁷ in 1910, diagnosed absence of the left lung from a roentgen-ray plate in a boy, aged ten years, who had a flattened left chest. It is possible that his case represents a true absence of one lung. But up to the present the clinical diagnosis of absence of a lung has never been verified at autopsy.

I desire to express my thanks to Dr. Carlos P. Chagas, of the pathological department, for having performed the autopsy and for having placed the literature on the subject at my disposal.

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SECONDARY MENINGITIS TREATED BY INTRASPINOUS ADMINISTRATION OF AUTOGENOUS SERUM. REPORT OF A CASE.

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DURING the last epidemic of influenza, some bronchopneumonia cases terminated in a fatal meningitis. These meningitides were reported to have been caused by pneumococci, various kinds of streptococci, and occasionally Bacillus influenzae.

Two such postinfluenza meningitis cases occurred in my ward at U. S. A. General Hospital No. 12. The second one was treated successfully by the intraspinal administration of autogenous serum. This is the case I am reporting, not only because of the favorable outcome, but also in order to have others try out this therapy.

REPORT OF CASE. Patient, L. S., No. 963, a plumber, was admitted from Camp Polk, N. C., December 10, 1918, to U. S. A. General Hospital No. 12, Biltmore, N. C., in a seemingly moribund condition. A history was not taken at this time because of his irrational and stuporous mental condition. However, on January 4, 1919, the following facts were obtained:

Personal History. About one whisky a day. Smokes fifteen cigarettes per diem. Otherwise negative.

Family History. Father died of sepsis from a carbuncle. Mother, one sister and a brother all alive and well. No history of any hereditary diseases obtained.

Past History. Had trouble with his left ear two years ago and says he does not hear well in that ear. He never had measles, mumps, scarlet fever, diphtheria, smallpox, pneumonia, meningitis or malaria. He denies venereal diseases by name and symptoms.

Present Illness (taken January 4, 1919). Onset of the present illness on December 1, with "a heavy cold," when he "coughed night and day." Also had a high fever. He was told at Camp Polk that he had pneumonia. Was admitted to U. S. A. General Hospital No. 12 on December 10.

Physical Examination. General condition: A dyspneic, cyanotic, toxic, stuporous and moribund white male, aged twenty years.

Skin and mucous membranes: No eruption; face flushed and drawn; eyes and pharynx congested.

Glandular system: No general adenopathy. No thyroid enlargement.

Vascular system: Pulse slow, regular, of good force and collapsible.

Heart: Not enlarged. No adventitious sounds.

Lungs: Bronchopneumonia, bilateral, disseminated (physical signs will appear below).

Genito-urinary System: Faint trace of albumin. Occasional granular cast.

Abdomen: Flaccid.

Liver: Reaches from fourth intercostal space to costal margin.

Spleen: Not palpable. No tenderness. No masses.

Nervous System: Negative except for stupor, which at times slips into semicomatose and at times changes to delirium.

Provisional Diagnosis. Bronchopneumonia, disseminated, bilateral, postinfluenzal. Sputum gave a questionable pneumococcus, type 2, precipitation test.

Progress. December 10. Conjunctivae congested. Laryngitis present. Voice hoarse and husky. Signs of bronchitis in lungs. Too

ill to examine thoroughly. Blood-pressure 100/55. Telegram sent: recovery doubtful.

Dec. 11. Condition not improved. Patient delirious. Vomited dark-green fluid. Given intravenously 1000 c.c. of a 5 per cent. glucose solution. We are testing out convalescent influenza, bronchopneumonia donors, who had a type 2 pneumococcus sputum, for a transfusion tomorrow. Blood count: White blood cells, 38,000; polymorphonuclears, 94 per cent.

Dec. 12. Transfusion of 500 c.c. of a convalescent postinfluenza, bronchopneumonia donor given by the sodium-citrate method by Lieut. A. Orth. Blood culture sterile.

Dec. 13. Patient is decidedly improved. Temperature 102°, pulse, 76, respiration, 26; whereas on admission temperature was over 105°, pulse 105, respiration 38. Signs in lungs of a disseminated bronchitis. Although consolidation is not definitely found, it probably exists. (Sputum culture showed Gram-positive diplococci; pneumococcus agglutination test gave a questionable positive type 2 reaction.)

Dec. 14. Condition improved markedly. Temperature 100°, pulse 64, respiration 24. Signs in chest diminishing. Telegram: improving.

Dec. 15. Temperature rose again to 103°. Signs in lungs as they were. Complains of a headache.

Dec. 17. Signs in right lower lobe posteriorly extending as far as the axilla still marked, but no absolute or classical evidence of consolidation. Temperature vacillating. Still complains of a headache.

Dec. 18. Patient is again irrational at times. Cardiovascular system in good condition. Lungs: crepitant and coarse moist rales heard almost everywhere. No definite signs of consolidation, though it probably exists. Nervous system: headache, photophobia, stiff neck, slight bilateral Kernig. Right knee-jerk almost absent. Left knee-jerk diminished. No Babinski, Oppenheim or Gordon. No clonus. Considering the temperature and signs of central nervous system, meningitis is probable. Telegram: recovery still doubtful. Blood culture again sterile.

Dec. 19. Temperature still septic. Blood-pressure 132/78, whereas on admission it was 100/55. Patient appears a little better. Neck still stiff. Kernig doubtful. Knee-jerk diminished. Not as irrational as yesterday. No headache, no hyperesthesia, no photophobia.

Dec. 20. At right base, posteriorly, there is now dulness, higher pitched breathing and crepitant and fine moist rales.

Neck stiff. Headache. Kernig positive. Lumbar puncture should not be deferred any longer. In afternoon lumbar puncture done; 40 c.c. of turbid, cloudy, purulent fluid, under increased tension, obtained.

EXAMINATION OF SPINAL FLUIDS.

Date, 1919.	Cell counts.	Globulin.	Colloidal gold.	Cultures.	Films.	Mouse inoculations.	Sugar.	Appearance.
Dec. 20	61,400 Polys. 93 per cent.	4+	2, 2 $\frac{1}{2}$, 2, 3, 4, 3, 3, 1, = 0, 0	No growth	Many Gram-pos. diplo- cocci, intra- and extra- cellular, resembling pneu- mococci	Fluid did not kill mouse	No reduction	Purulent.
Dec. 23	No growth	Purulent.
Dec. 25	31,800 per cmm.	No growth	Purulent.
Dec. 26	No growth	Widened of 20 c.c. of fluid did not kill mouse	Purulent.
Dec. 27	415	No growth	No effect on mouse	Yellow, less cloudy, (clearer.
Dec. 28	No growth	Moderate number of pus cells and occasional gram + diplococci. No tuber- culosis
Dec. 30	600	No bacteria found	Normal tension per- ceptibility clearer. (clear yellow fluid.
Jan. 1	300	No growth	No bacteria; pus cells; oc- casional red blood cells
Jan. 2	240	No growth	Clear yellow.
Jan. 6	20	=	No growth	Clear yellow.
Jan. 15	13	=	1 $\frac{1}{2}$, 2, 2, 2, 1, 0, 0, 0, 0	No growth	Reduction	Clear aqueous.

OTHER LABORATORY FINDINGS.

Blood cultures sterile Dec. 12, 18, 21 and 27.

Jan. 12. Pus from parotid duct = *Staphylococcus aureus* and *Streptococcus viridians*. Mouse did not die from broth inoculation of the latter.

Sputum: For type of pneumococcus; no definite agglutination. Not bile soluble.

Urine precipitation test for type pneumococcus, negative.

Wassermann, 1 plus.

Blood Counts—Dec. 10: White blood cells, 38,300; polymorphs, 94 per cent.

Dec. 20: White blood cells, 26,900; polymorphs, 90 per cent.

Jan. 4: White blood cells, 21,200; polymorphs, 66 per cent.

Spinal Fluid:

Cell count, 61,400.

Differential count: polymorphonuclears, 93; lymphocytes, 7.

Globulin, 4 plus.

Colloidal gold reaction.

Test-tube No. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 control.

Result: 2, $2\frac{1}{2}$, 2, 3, 4, 3, 3, 1, =, 0, 0.

Sugar reduction test, negative.

Culture, no growth.

Original film showed gram + diplococci, both resembling pneumococci, intracellular and extracellular.

Mouse inoculation, mouse remained alive.

Blood count: White blood cells, 26,900; polymorphonuclears, 90 per cent.

Dec. 21 (family present). Lumbar puncture done again this morning; 45 c.c. of cloudy fluid removed. Patient is apparently slightly improved. In afternoon lumbar puncture, 40 c.c. of cloudy fluid under less tension than that previously removed. Retinoscopy: Bilateral edematous papillitis (choked disk). Blood culture, sterile.

Dec. 22. Lumbar puncture done twice today.

Dec. 23. No headache. Neck not so stiff. In afternoon lumbar puncture done; 33 c.c. of cloudy fluid withdrawn. An autogenous serum for intraspinal treatment is being prepared. The patient evidently has immune bodies in his blood, for he is overcoming the pulmonic process. Culture of spinal fluid on blood agar, blood broth and serum broth negative.

Dec. 24. Left lung posteriorly, crepitant and moist rales. Right lung, lower lobe, is still consolidated. At 11 A.M. lumbar puncture. 40 c.c. of pus-laden fluid withdrawn. Injected 15 c.c. of autogenous serum. At 9 P.M. lumbar puncture repeated. 60 c.c. of less cloudy, yellowish fluid drained off. Injected 15 c.c. of autogenous serum.

Dec. 25. Lumbar puncture done twice today and autogenous serum injected. Examination of spinal fluid showed quantity 42 c.c., cell count 31,800, culture again negative.

Dec. 26. Lumbar puncture done and serum given twice today. Mouse inoculation twice with the sediment from 20 c.c. of spinal fluid did not kill the animal.

Dec. 27. Lumbar puncture repeated. 25 c.c. of autogenous serum administered. Spinal fluid is now yellowish from the serum and a little less cloudy perhaps. However, the general condition of the patient is worse. He is irrational. Blood culture again sterile.

Dec. 28. Although the temperature is persistently decreasing under the use of autogenous serum, the general condition of the patient is worse. He is now stuporous and irrational, but the vegetative organs seem to be holding up well. Mouse inoculation with the sediment of 30 c.c. of centrifugalized spinal fluid showed no effect on the mouse. Culture of the spinal fluid on blood agar and

blood broth sterile. Smear showed moderate number of pus cells and occasional Gram-positive diplococci. Smear for tuberculosis negative.

Dec. 29. Transfusion of 450 c.c. from a convalescent, post-influenzal, bronchopneumonia donor done by the sodium-citrate method. This was deemed necessary because the patient has been repeatedly bled in order to make up autogenous serum and because of the benefit of the last transfusion. Serum treatment twice today. Temperature has slowly declined until now it vacillates between 99° and 100°.

Dec. 30. Lumbar puncture. Spinal fluid: 600 cells per c.mm. Bacteria negative.

Dec. 31. Temperature normal. Patient appears less stuporous, but he is still irrational. Examination of left lung shows it almost clear and resonant. Lumbar puncture showed the fluid under normal tension and for the first time perceptibly clearer. It has, of course, a yellow hue from the serum. All in all the prognosis is more encouraging. Spinal fluid: cell count, 415 per c.mm.

Jan. 1. Patient is no longer irrational. Neck is not stiff. Kernig, however, still positive. Pupils dilated. Pulse: lower tension and dirotic. Appetite very good. Lumbar puncture done and 25 c.c. of clear, yellowish fluid removed under normal tension. 20 c.c. of autogenous serum injected into the spinal canal. A clear fluid corroborated the clinical symptoms of marked improvement. Spinal fluid: 300 cells per c.mm. Smear: Bacteria negative, occasional pus cell. Few red blood cells. Culture negative.

Jan. 2. Lumbar puncture, 240 cells per c.mm. autogenous serum administered.

Jan. 3. Still delirious at times, but neck is no longer stiff. Kernig is still positive. Knee-jerk unequal. Lumbar puncture: Canal entered and blood was withdrawn twice. No serum given. Temperature under 100°.

Jan. 4. Neurological and mental status. Cranial nerves are normal. Somatic nerves: no anesthesia, no paralysis. Reflexes; pupils dilated; both react to accommodation. Right pupil reacts sluggishly and slightly to light; left reacts less sluggishly. Bicipital and tricripital reflexes normal. Pectoral, abdominal and cremasteric reflexes normal. Right knee-jerk absent. Left knee-jerk diminished. Neck still slightly stiff. Kernig sign still positive. Achilles and patella reflexes normal. No Babinski, Oppenheim or Gordon.

Perception: Fairly good but a little hazy. He recognizes and knows the use of common objects. He is oriented as to time fairly accurately, but is perfectly oriented as to place and person. No hallucinations exist. He does not dream.

Memory: He recalls well school days, date of enlistment and military life.

Emotionally stable.

Judgment and reason good. In case of fire he says he would wait for help. Were he able he says he would run with water-buckets to the fire. Lately he had been occasionally delirious. Only when delirious from pneumonia, pyrexia and meningitis did he show delusions and confusion. Then he talked about his wife, although he is single. However, he says he is now engaged.

Volition: Rather apathetic. Can feed himself, he says, but nurse does it for him. Involuntary defecation and micturition exists.

Attention: Is good.

Train of thought is coherent.

All in all, he is fast approaching normal mentality. The prognosis for a complete mental recovery is good. Blood count: white blood cells, 21,200. Polymorphonuclears, 66 per cent.

Jan. 5. Patient's temperature around 99°. He feels good. Pulse 100. Patient has bleeding hemorrhoids; a small indurated swelling is presenting itself below the mastoid process, just behind the right ear. Because the pulse has become more rapid, because the patient has been repeatedly bled for autogenous serum, and because of bleeding hemorrhoids and epistaxis from picking his nose, and because of the cervical infection, a blood transfusion of 500 c.c. was again done by the sodium-citrate method.

Jan. 6. Lumbar puncture done. 30 c.c. of rather clear fluid under increased tension removed. 22 c.c. of autogenous serum administered. Spinal fluid: 20 cells per c.mm. Globulin test: slight precipitate. Culture, negative.

Jan. 7. The swelling and inflammation of tissue below the right ear is more superficial and spreading. Urine: Pneumococcus precipitation test; no precipitation.

Jan. 8. Right ear-drum shows a prominent malleus with blood-vessels running down along it. Moreover, all around the margin of the drum vessels are migrating toward the center. Retinoscopy shows choked disk less severe than previously; also what appears to be an exudative retinitis.

Jan. 9. The swelling has grown larger and has spread and involves the whole parotid gland. It is red, hot, indurated and tender. There is no fluctuation. The temperature has risen, but this is due to the parotid inflammation, not the meningitis, which is practically cured. Eyes still staring. Kernig present. The hemorrhoids have bled considerably and he seems to pick at them.

Jan. 10. Swelling has now involved the whole right parotid. On gentle massage a bead of pearly pus presented at the orifice of Stenson's duct.

Jan. 11. Parotitis still the same. Temperature dropped. Kernig still present. Lungs seem clear.

Jan. 12. Parotid not so swollen nor so tender. Temperature is normal. Stenson's duct is still patent and a drop of yellow pus can

be pressed through the pouty orifice. Kernig sign is much less marked. Head not stiff. Mind is clear. Culture of pus from Stenson's duct showed a *Pneumococcus-streptococcus viridans* and a *Staphylococcus aureus*.

Jan. 13. Swelling of gland is decreasing. Pus can be expressed at will through the oral orifice.

Jan. 14. Parotid swelling decreasing, orifice less pouty and from it drains creamy pus.

Jan. 15. Parotid swelling nearly all gone. Pressure on the gland causes pus to be evacuated through the mouth.

Jan. 23. Lumbar puncture done. 25 c.c. of clear, aqueous solution withdrawn.

Spinal Fluid:

1. 13 cells per c.mm.

2. Globulin: plus-minus.

3. Colloidal gold reaction.

Test tubes Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 control.

Result: $1\frac{1}{2}$, 2, 2, $2\frac{1}{2}$, 2, 1, 0, 0, 0, 0.

4. Sugar, faint reduction.

Jan. 25. Patient feels fine. Appetite is splendid. Bowels regular. He is permitted to go to the bathroom. Temperature, normal.

Neck limber. Parotid swelling completely gone. Kernig negative. Right knee-jerk greatly diminished, only evident when reinforced. Left knee-jerk diminished to a lesser extent.

Retinoscopy: The papillitis and retinitis have disappeared. Fundi now appear normal.

The right ear-drum, which was hyperemic when the parotitis existed, has also returned to its normal appearance.

(These notes are taken verbatim from Clinical Record No. 963-1925, U. S. A. General Hospital No. 12.)

The subsequent notes are condensed and will show an uneventful recovery.

Jan. 31 to Feb. 4. Patient ran a low-grade afternoon temperature, evidently due to slight exertion.

April 10. Neurological and mental examination negative.

April 29. Physical examination showed defective hearing in left ear. He may be discharged on certificate of disability. Meanwhile patient had been on graded exercises, as were all convalescent patients.

A note by a specialist said: Hearing, right ear, 9'20; left ear, 0'200.

Diagnosis: Partial deafness in left ear, probably of central origin and exaggerated as to degree.

DETAILS FOR PREPARATION AND ADMINISTRATION OF AUTOGENOUS SERUM. Aseptically insert a needle into the median basilic vein of the patient at the elbow and draw off blood into four

50 c.c. centrifuge tubes. Separate the clot with a flamed platinum needle and centrifuge carefully at low velocity. After the serum is separated the tubes are kept in the ice-box. Centrifuging is not absolutely necessary if the serum separates easily. The spinal canal is tapped in the usual manner with the Quincke needle and spinal fluid is allowed to flow off slowly. About 30 to 60 c.c. of the turbid fluid is drawn off; the amount, of course, depends upon the spinal pressure and the clinical condition of the patient. The clear serum, which had previously been warmed to body temperature, is drawn into a 50 c.c. Luers syringe and injected into the spinal canal. Then the foot of the bed is raised.

Lumbar puncture and administration of serum should be done morning and night until the temperature drops. Then it should be done once a day; eventually on every second day and thus gradually decreased according to the clinical course of the disease and the laboratory examination of the spinal fluid.

DISCUSSION. The rationale of autogenous serum therapy in secondary meningitis is evident for the following reasons:

1. Immune bodies exist in the serum in practically all infectious diseases.

2. This immune serum is brought into direct contact with the inflamed meninges and with the offending microorganisms.

3. Ordinarily the choroid plexus bars the free passage of immune bodies from the blood to the spinal fluid.

The principle suggested itself in this case because the patient was slowly overcoming the pneumonic process when the meningitis occurred. It was logical to suppose that he had immune bodies in his serum.

It is interesting to analyze this case more thoroughly and to evaluate the various procedures.

Upon admission the moribund pneumonic patient was literally revitalized by the timely use of three common therapeutic measures.

1. An infusion of 1000 c.c. of 5 per cent. of glucose solution which caused elimination by diuresis, increased cardiac function and had nutritional value.

2. Immune blood transfusion on the second day, which acted as a stimulant, and as a neutralizer of the toxemia.

3. Cardiac stimulation with caffeine sodium benzoate, digitalin and camphor oil, alternatively, every six hours.

The patient, with the help of these therapeutic methods, was successfully combating the pneumonia; the temperature was stepping down; the leukocytosis was high; the whole clinical condition was improving remarkably when the meningitis started.

After the meningeal infection had gained headway, lumbar puncture *per se* was life-saving, because it relieved the otherwise fatal intracranial compression and because it drained the purulent toxic spinal fluid. Whether rachicentesis alone with the natural

and transfused immunity would have cured the meningitis, no one can say. The fact is that six days after the treatment with the intraspinal autogenous serum the temperature was normal. Although the patient seemed somewhat better just before the spinal treatment was instituted, we all know how misleading those apparent improvements in meningitis cases actually are; recurrences are the rule. Even from a hypercritical and conservative standpoint we can justly state the result is suggestive. It undoubtedly seems to have been beneficial in this case and may possibly aid in others. It cannot be denied that it is a very rational therapy and therefore should be tried in the absence of a specific immune serum of known value.

The unilateral suppurative parotitis was an unusual complication. The culture of the pus showed a *Staphylococcus aureus* and a Gram-positive diplococcus belonging to the *Pneumococcus-streptococcus viridans* group. This was probably not a hematogenous but an ascending duct infection, as four blood cultures were negative. The orifice of the duct was always patent and always drained pus until resolution occurred without surgical interference. No apparent parenchymatous destruction of the gland took place.

Three 500 c.c. transfusions were given. All the donors were convalescent influenza Bronchopneumonia patients. All were infected, as was this patient, at Camp Polk. The first transfusion was given to combat the pneumonia and the concomitant toxemia. The second was given to make up the blood withdrawn to prepare the autogenous serum. The third was given for the same reason and because blood was lost by epistaxis and bleeding hemorrhoids; then, too, it cut down the convalescence and may have helped the parotitis.

LABORATORY DISCUSSION. I have delayed publishing this article because I should have preferred to have had Capt. A. L. Garbat, M. D., New York City, chief of the laboratory, discuss this subject. However, he has been ill and hence unable to contribute his part.

It was unfortunate that no absolute conclusion could be reached as to the type of organism we were dealing with in the meningeal infection. The sputum gave a doubtful capital group 2 agglutination by the mouse method, but the organisms were not bile-soluble. The urine showed no precipitation tests. Repeated cultures from the turbid spinal fluid made on all types of plain blood or serum media remained sterile. Repeated animal inoculations with the sediment of the spinal fluid did not kill the mice, although stained specimens of the sediment showed definite Gram-positive diplococci both intra- and extracellular which had the morphology of pneumococci. Apparently the bacteria were dead. Smears from the pus of the parotid showed a similar organism, but these bacteria grew rapidly on artificial media, with the characteristics of a *Streptococcus viridans*. The cultures produced green pigment on blood agar, were bile-insoluble, were not agglutinated by pneumococcus serum and did not kill mice. Naturally one cannot draw any definite con-

clusions as to the nature of the meningeal infection from these findings. This does not, however, materially influence the point of importance which the author desired to bring out, namely, that it is wise in secondary meningitis to use intraspinally the autogenous serum, which probably contains a number of antibodies from the primary infection.

CONCLUSION. We recommend the use of autogenous serum injected into the subarachnoid space in cases of secondary meningitis when there is no efficient specific immune serum.

I must take this opportunity to thank Capt. A. L. Garbat, chief of the laboratory of U. S. A. General Hospital No. 12 for his ever-helpful coöperation. I also appreciate the assistance given by Sgt. P. Piel and his brother Pvt. R. Piel, of the laboratory force, who carefully made up the autogenous serum under our direction.

OBSERVATIONS ON THE COLLOIDAL GOLD REACTION WITH CEREBROSPINAL FLUID.

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DURING the past four years the colloidal gold test on cerebrospinal fluid as devised by Carl Lange has aroused great interest among physicians and laboratory workers. This reaction, the exact nature of which is not yet clearly understood, is proving of some practical value as a diagnostic procedure. The utility of the test is not generally recognized at the present time, and frequently the reaction yields information not obtained so quickly by any other diagnostic measure. This is seen particularly in the occasional case of meningitis in which the Wassermann reaction is negative and a characteristic curve is obtained by the colloidal gold method, or where a tuberculous curve is obtained and no acid-fast bacilli found; also in cases in which differential diagnosis between poliomyelitis and tuberculous meningitis is difficult the reaction has proved of value. As in all laboratory diagnostic procedures, however, occasional false reactions are obtained, and it is the chief object of this paper to record a few such instances and to make certain observations which may prove of interest to those performing the test.

Previous articles on the gold reaction have considered in great detail the methods of preparing the fluid, and we shall not discuss the subject except to say that if directions regarding cleanliness of glassware and purity of reagents are carefully adhered to no great

difficulty will be experienced in making the colloidal gold. Colloidal fluids will vary in their physical characteristics, and occasionally the same spinal fluid will give, with different colloidal gold solutions, a slightly variable curve, but the results are usually comparable. Nevertheless, it is advisable to use spinal fluid from known cases as a control to check the accuracy of each new lot of colloidal gold. Fluids that are opalescent yield a more marked curve than others, but although exaggerated the curve can usually be interpreted. Conversely, fluids having a clear red appearance and no trace of opalescence may yield but slight and inconclusive reactions. Such fluids are much more permanent than those possessing some degree of opalescence. In preparing the fluid it will be found that quantities of 500 c.c. or less are more readily prepared than larger amounts, and because of the ease of manipulation, this quantity is recommended or smaller quantities when few specimens are received.

NEGATIVE TESTS. In our experience the curves obtained in tuberculous and syphilitic meningitis and in tabes have been similar to those described by others. No correlation could be made between the degree of the curve and the extent of pathological involvement, but the fluid from patients with tuberculous meningitis gave an exceedingly pronounced curve when examined several days before death. In fact the reactions might be termed atypical, in that they tended to show the greatest change in the terminal tubes. Such fluids also showed a greatly increased cell count and positive globulin reaction, and the extent of the curve seemed to run parallel with the amount of globulin present estimated by the Noguchi butyric acid method. In a series of seventy-five fluids giving negative colloidal gold reactions only three showed a positive globulin test and increased cell count. They were as follows: one of syphilis, one of poliomyelitis and one of tuberculous meningitis. Thus the reaction failed in 4 per cent. of fluids that were obtained from known cases positive by other methods. In other instances of negative curve and positive globulin test, blood in greater or lesser quantity was found on microscopic examination. In the examination of the centrifugalized sediment it is highly important, in determining the presence of blood, to examine a fresh, unstained drop for very often in routine work the presence of a moderate number of erythrocytes is not demonstrated by the staining methods ordinarily used. The erythrocytes do not stain well or are washed off during the various manipulations. In our seventy-five negative fluids, which included a variety of conditions, there were three which gave positive Wassermann reactions and two others giving negative Wassermann tests, though the blood in both these cases yielded positive Wassermann reactions. These latter fluids reacted negatively by all other methods. The colloidal gold test, therefore, failed to react in 7 per cent. of positive cases.

SYPHILIS. Fairly constant reactions were obtained in syphilis, but there was great variation in the extent of the curves, and here, again, it appeared that the most marked reactions gave the strongest globulin tests. In a total of 122 luetic curves of varying degree there were obtained 95 giving changes that could be regarded as positive or highly suggestive of syphilis. Of these 62, or 70 per cent., gave positive Wassermann reactions, and of the remainder, 24 per cent., could be excluded as probably not syphilitic. There thus remained 6 per cent. of specimens when the colloidal gold test was positive and the Wassermann reaction negative. These cases were syphilis clinically. In 22 per cent. of the fluids the curves could not be interpreted, being either slight or else irregularly exaggerated. These figures would indicate that while the method appears to be more sensitive than the Wassermann test, there is much greater possibility of error in the absence of confirmation by other methods.

TUBERCULOSIS. Forty cerebrospinal fluids were received which gave positive colloidal gold curves and in which the tentative clinical diagnosis of tuberculous meningitis was made. Of these, 7 were subsequently excluded as not tuberculous. There thus remained 33 cases of tuberculous meningitis corroborated by other tests, guinea-pig inoculations or postmortem examinations. All these fluids yielded a negative Wassermann reaction, but had an increased cell content and globulin. Of the 33 known cases, 4 gave curves suggesting acute meningitis. Thus the reaction was correct in 88 per cent., and misleading in 12 per cent. The four fluids yielding acute curves were from terminal cases, and all showed a greatly increased cell count, strongly positive butyric acid test and tubercle bacilli in smears. Guinea-pigs were also positive for tuberculosis.

ACUTE MENINGITIS. Fluids from 27 cases of acute meningitis were examined and 20, or 74 per cent., gave curves suggesting acute meningitis. Thus 26 per cent. were negative or inconclusive. In all these specimens the organisms were demonstrated in smears or cultures except one. In addition to the meningococcus there was 1 case of pneumococcus meningitis and 1 of *Bacillus mucosus capsulatus* infection. The latter reacted negatively. One fluid gave a curve in the luetic zone and 3 others were difficult to distinguish from tuberculous curves. The one fluid in which no organisms were found and which did not yield a characteristic curve showed a strongly positive globulin test, heavy sediment of polynuclear leukocytes and no reduction of Fehling's solution. This patient, a young woman of sixteen years, had been ill two weeks and subsequently became well without serum treatment.

Thus we find the reaction confirmatory in approximately 80 per cent. of cases. It apparently is most valuable in cerebrospinal syphilis, for many positive results are obtained when the complement-fixation reaction is negative. These results, however, unless confirmed by positive globulin tests and increased cell count,

should not form the basis for intraspinal or intravenous medication, but should lead to very careful observation of the patient and repeated examination of the fluid. In tuberculous meningitis the chief value of the reaction lies in the fact that a majority of these cases may quickly be distinguished from poliomyelitis in children and syphilis in adults. It thus also becomes valuable from a prognostic standpoint, but guinea-pig inoculation should not be neglected even in such instances. In acute meningitis the other changes are of much greater importance. It is rather interesting to note that in tuberculous meningitis when the exudate becomes very profuse the gold curve suggests acute meningitis. Differential diagnosis at this time would be difficult without the presence of organisms in smears. In poliomyelitis we found the curve inconstant, but more often in the luetic zone. In a number of instances in which the condition could not be differentiated clinically the curve was misleading. A few of the more interesting of these cases are cited below.

CASE I.—Mr. H. J., aged forty-two years. Chief symptoms: mental confusion; marked headache; retraction of head; bilateral optic neuritis; slight nystagmus, chiefly to left; reflexes weakened; evening temperature. The clinical diagnosis was meningitis. Four specimens of spinal fluid were received over a period of twenty three days, with the following results:

	Globulin.	Cell count	Smears.	Wassermann	Colloidal gold.
1	Positive	...	Increased number of cells, few mononuclears and many polynuclears, few erythrocytes	Negative	0035554300
2	Positive	460	do. do.	Negative	1543333210
3	Positive	360	do. do.	Negative	0034543100
4	Positive	340	do. do.	Negative	0014544333

No organisms were found in smears, cultures were sterile and guinea-pigs inoculated showed no evidence of tuberculosis. The patient died and the autopsy disclosed a subacute endocarditis involving the mitral valve and numerous infarctions of the brain. In this case the curves obtained were entirely misleading. At different times tuberculosis, syphilis and acute meningitis were suggested.

CASE II.—George K., aged two years. Clinical diagnosis: acute meningitis. The patient presented the usual symptoms of acute meningitis. The first spinal fluid received was very turbid; globulin strongly positive; cell count, 140. Wassermann negative. The sediment showed numerous small and large mononuclear cells, polynuclears and no organisms. The following gold curve was obtained: 0123344554. A similar result was obtained seventeen days later, but acid-fast bacilli were also found. The patient died and the autopsy disclosed tuberculous meningitis, with a very extensive exudate at the base of the brain. This, therefore, was a

case of tuberculous meningitis, but the colloidal gold curve suggested acute meningitis.

CASE III.—Miss B., aged seventeen years. Eight weeks after operation for middle-ear abscess the patient developed intense headache; increased reflexes; temperature 100° to 100.5° F.; photophobia. Five specimens of spinal fluid and one of blood examined over a period of one month gave negative Wassermann reactions. The globulin reactin was strongly positive and the sediments showed greatly increased numbers of lymphocytes. The colloidal gold reaction persistently suggested syphilis, giving curves of which the following is an example, 5544311100. Six guinea-pigs inoculated with different specimens of spinal fluid gave negative results. The patient died shortly after, but no autopsy could be obtained. The history and termination suggested cerebral abscess, but the colloidal gold test suggested tabes.

CASE IV.—Mrs. C. P., aged forty-four years. Clinical diagnosis not made. Syphilis suspected. Chief symptoms: headache; vomiting; inability to walk; exaggerated reflexes; weakness. Temperature, 97° F. "The Wassermann reaction was reported negative by two different laboratories." The cell count and globulin were increased and the colloidal gold reaction gave the following curve—2345542000—thus suggesting syphilis. About six weeks later the patient died. The history and physical signs in this case suggested cerebral tumor. No autopsy could be obtained.

CASE V.—The following data are of interest as an illustration of the effect of intraspinal medication. Mr. G., aged forty-five years. Primary lesion seventeen years previously. Symptoms at present suggest taboparesis.

Date.	Globulin.	Wassermann.	Cell count.	Colloidal gold
June 9	Positive	++++	250	4555543100
22	Positive	++++	Greatly increased	2345554310
July 12	Positive	+++	25	0001322210
20	Positive	++	Slight increase	3333200000
Aug. 3	Negative	80	0000000000
Sept. 1	Weakly positive	++++	3333300000
21	Positive	++++	Increased	1133331110
Nov. 17	Positive	+++		
Dec. 19	Weakly positive	++	Increased	1333331000

This patient received numerous intraspinal injections of salvarsanized serum and intramuscular injections of mercury salicylate. The treatment appeared to have but slight permanent action on the syphilitic process. It is interesting to note that the extent of the colloidal gold curves remained in keeping with the Wassermann reaction and the globulin test.

CASE VI.—Mr. T. H., aged forty years. Died, after several days' illness, with symptoms suggesting meningitis. At autopsy there was found acute pancreatitis and intense edema of the brain. The cerebrospinal fluid removed at autopsy gave the following curve—113455552—thus suggesting acute meningitis. Otherwise the fluid was negative.

CASE VII.—T. N., aged three years. Symptoms of acute meningitis. The cerebrospinal fluid showed 1100 cells per cubic centimeter, strongly positive globulin test and negative Wassermann reaction. The sediment yielded greatly increased numbers of lymphocytes and polynuclear leukocytes; acid-fast bacilli present. The colloidal gold reaction performed, with two specimens of fluid collected on different days gave negative results. Guinea-pigs were positive for tuberculosis.

CASE VIII.—Miss C. E., aged twenty years. After preliminary malaise, anorexia, headache and mental dulness the patient rapidly developed symptoms of acute meningeal disturbance, with marked retraction of head, rigidity of spine, hyperflexion of legs and thighs in lateral decubitus and progressively increasing stupor. The pupils were immobile, but there was no definite strabismus. Clinical diagnosis: tuberculous meningitis.

The spinal fluid showed greatly increased number of lymphocytes, positive globulin reaction (double plus) and negative Wassermann. The colloidal gold curve suggested syphilis. Guinea-pigs reacted positively for tuberculosis.

CASE IX.—Miss N., aged twelve years. Complete paraplegia below the fourth cervical segment; slow onset; three months' duration. No sensory disturbances. Electrical reactions present. Cerebrospinal fluid under pressure, clear; cell count, ten; globulin strongly positive. Wassermann reaction negative. Colloidal gold curve 1223331100, suggesting syphilis. Clinical diagnosis: poliomyelitis.

CASE X.—Mr. E. C., aged thirty years. Influenza two weeks previously. Entered the hospital complaining of headache, vertigo and vomiting. Temperature, 97° F.; pulse, 50. Two days later he became restless and delirious. Axillary temperature, 100° F.; pulse, 120; slight retraction of head; twitching of arms and legs, especially on the left side. Respiration rapid and of Cheyne-Stokes type.

The cerebrospinal fluid removed just prior to the onset of the latter symptoms contained eight cells per cubic centimeter; globulin double plus; no reduction of Fehling's solution and a negative Wassermann reaction. Smears showed mononuclears chiefly. No organisms were found. The colloidal gold reaction gave the following curve—0133322100. The patient died and the autopsy disclosed a diffuse glioma involving the right parietal region.

BLOOD CONTAMINATION. Perhaps one of the most serious faults in the test lies in the fact that cerebrospinal fluids when contaminated with blood yield curves in the luetic zone, thus making interpretation very difficult. A relatively small quantity of blood serum appears to be sufficient to produce marked reactions. To determine precisely this effect, human serum in varying dilutions was tested with colloidal gold and found to yield curves in the luetic zone. The curves were most typical in a 1 to 1000 dilution, and this quantity of serum is sufficient to give a plus minus or a one plus globulin reaction. In routine work a large proportion of spinal fluids contain a trace of blood, and if not carefully guarded against, serious errors of interpretation may result. Human serum in very low dilution gives curves in the terminal or acute meningitic zone. Diluted luetic serum appears to give more pronounced curves than the non-luetic serum and inactivation does not greatly alter the curves. The following is an example of the gold solution reactions obtained with human serum:

Serum.	Globulin	Colloidal gold.
Undiluted 0.2 c.c.	0001232222
1 to 100	++++	2223422020
1 to 1000	+	3443320000
1 to 10,000	0	1100000000

Although it is preferable to perform the reaction with fresh fluid, yet it was found that specimens kept several weeks at ice-box temperature yielded a characteristic but slightly diminished curve. The heating of fluids caused slight change in the curves even when the spinal fluid was heated to the boiling-point. The few observations made with contaminated fluids show that such specimens are unsuited for examination, for frequently reactions are obtained in the luetic zone when all other tests are negative.

CONCLUSIONS. 1. The colloidal gold reaction is useful as an additional or confirmatory test.

2. It is of greatest value in the syphilitic diseases of the central nervous system, especially tabes and paresis.

3. The test may serve to differentiate between tuberculous and other forms of meningitis.

4. The reaction is correct in approximately 80 per cent. of cases.

5. Cerebrospinal fluid contaminated with blood in small quantity frequently gives reactions in the luetic zone.

6. Positive results unconfirmed by other tests are of only slight value.

7. The Wassermann reaction and the cytological examination of the cerebrospinal fluid are of greater value than the colloidal gold test.

THE PREPARATION OF A STABLE VITAMINE PRODUCT AND ITS VALUE IN NUTRITION.*

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AND

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INTRODUCTORY. The view is no longer accepted that a diet of purified proteins, fats, carbohydrates and mineral salts in proper proportions is adequate for the needs of the body. In 1911, Funk¹ obtained from rice polishings and yeast a substance which he called "vitamine." This substance could prevent and cure beriberi, or its analogue polyneuritis, in birds, and was therefore called "antineuritic vitamine." Subsequently, Funk,² Hopkins,³ and others showed that this vitamine, found in a variety of grains, vegetables and animal products when added to such a diet as the above makes it satisfactory for growth. Funk⁴ expressed the view that there is besides the antineuritic vitamine a separate and distinct antiscorbutic vitamine distributed in fruits and vegetables and a specific antirachitic vitamine occurring in certain animal fats and oils.

Regarding the value in nutrition of the vitamins as they occur in the natural fresh foodstuffs, it has been demonstrated, time and again, of what vital importance they are to satisfactory maintenance and growth. However, owing to prevailing methods of food preparation, such as refining, heating, drying or canning, the activity of the vitamins is largely destroyed, with the result that continued ingestion of such food, even though eaten in sufficient quantities to satisfy the appetite, may ultimately lead to the various nutritional disturbances caused by a lack of vitamins in the diet. When one considers the minute amount in which vitamins are normally present in an adequate diet the extent of their nutritive value becomes the more remarkable.

It is known that disturbances in health may exist without arriving at the extreme stage when the appearance of a severe set of symptoms leads to the recognition of actual disease. This is particularly true of malnutrition which may arise irrespective of the quantity of food eaten. Malnutrition depends not upon

* Read before the Division of Biological Chemistry at the Fall meeting of the American Chemical Society, Philadelphia, Pa., September 5, 1919. We are indebted to Mr. H. A. Metz for the many facilities placed at our disposal during the course of this investigation.

insufficient food but upon improperly prepared foods or upon an improper combination of foods. The essential thing to recognize is that absence of vitamins from the food means disease and that a partial deficiency of vitamins leads to poor nutrition. Particular attention should likewise be paid to the diet of nursing mothers. Because of the inability of the body to synthesize its own vitamins, it is of prime necessity that the nursing mother shall partake of such a diet as will ensure an adequate supply of vitamins so that her milk will constitute a satisfactory food for the baby. If sufficient vitamins are not obtained in the usual diet then the deficiency must be supplied in some other way, as suggested by Voegtlin.⁵

Discussing the importance of vitamins in relation to nutrition in health and disease, Voegtlin⁵ says: "It is of great importance that vitamin preparations should become available for the practising physician for the treatment of deficiency diseases. It is quite possible that a number of indefinite complaints and symptoms of adults and infants may be due to a partially deficient diet and would be benefited by the administration of vitamins. It is not always necessary that the full picture of a deficiency disease make its appearance. Such vague symptoms as loss of appetite and general weakness might very well, in some instances, be due to a deficient diet."

Proceeding from the above premises it was thought desirable to try to prepare a stable vitamin product that would prove effective therapeutically in increasing body growth whenever the nutritive powers of the individual were below par. After extended investigation we succeeded in preparing an active vitamin product, which we shall designate as vitamin preparation "V," the constitution of which we shall discuss in detail later on.

Experimenting with pigeons⁶ we found that 1 gram of the vitamin product given every other day in addition to polished rice was sufficient (*a*) to prevent the onset of polyneuritis, (*b*) to cure polyneuritis and (*c*) to maintain and increase body weight. It subsequently developed that the amount of vitamin preparation fed to the pigeons was considerably greater than was actually required. Encouraged by these results we decided to determine the effect of feeding the vitamin preparation to children exhibiting a condition that could be attributed to a lack of vitamins in the diet. The cases available for study included children showing evidences of malnutrition, marasmus and rickets. We understand, of course, that the term "malnutrition" describes a symptom rather than a disease, but when no pathological reason exists to account for the malnutrition we may properly treat it as a dietary deficiency.

PLAN OF EXPERIMENT.

The experiment was divided into two parts: Part A, using four children, and Part B, using ten children. The babies selected were placed in separate cubicles under the constant supervision of day and night nurses. All food was carefully weighed or measured, so that the exact amount eaten was known. In addition to recording the weights of the babies every other day we ran a nitrogen, phosphorus and calcium balance, hoping thereby to note any possible deviation from the normal as a result of added vitaminic ingestion.

Part A. This part of the experiment, which included the nitrogen, calcium and phosphorus balance, was divided into three periods: (I) Fore period of from nineteen to twenty-two days; (II) vitaminic-feeding period of twenty-eight days, during which the children received 1 gram of the vitaminic preparation daily in addition to their usual diet; (III) after a period of twenty-one days. After many trials a suitable method was devised whereby quantitative collections of urine and feces were made, the latter being marked off by carmin. Such collections were made during the last eight days, but three of Period I, the last six days of Period II and the last five days of Period III. Analyses were made by the usual well-known methods.

Part B. Here we have two periods: (I) Fore period of from ten to thirty-nine days and (II) vitaminic-feeding period of forty days, during which five of the children received 1 gram of the vitaminic preparation daily in addition to their usual diet, while the other five, receiving their diet only, acted as controls. During the last seven days of Period II, 2 grams of the vitaminic preparation were given daily, and at times orange-juice was given, but nothing of particular import was observed as a result of this extra feeding.

It should be noted here that at the beginning of the fore period all these babies were given suitable formulas according to their needs. These formulas were changed from time to time in regard to their protein, fat and carbohydrate content when it appeared necessary, as shown in Table VII. Naturally during the fore period some of the babies thrived better than others. At the end of the fore period those babies which had done well were divided into two lots, and those babies which had not done so well were likewise divided into two lots. One lot of the "good" babies was combined with one lot of the "bad" babies, and the resulting lot of five babies (Lot V) was given the vitaminic product in addition to the regular diet. The remaining lot of five babies (Lot C) received their usual diet only, and in this way acted as a basis of comparison for the first lot of children.

HISTORY OF PATIENTS.

Part A. Paul P. was admitted to the hospital November 22, 1918, aged fifteen months. He appeared to be very ill, was poorly developed, with flabby and wasted muscles. A diagnosis of marasmus was made and a suitable diet was prescribed. On January 15, 1919, the child weighed 14 pounds and its condition remained poor. On March 16 he was placed on a diet of bread, butter, milk, cereal and a mixture consisting of four eggs, 400 c.c. milk, 5 gm. sugar and 2 gm. common salt. The experiment began March 19; weight, 14 pounds; age, nineteen months.

William D. was admitted to the hospital February 26, 1919, aged thirteen months. He had an infection of the left hand and a discharge from the nose which persisted from the beginning of the experiment until March 29. The general condition of the child was poor, the muscles were flabby and he was poorly developed. A diagnosis of rickets was made. The child had been getting whole milk, and this diet was discontinued throughout the experiment, which began March 22, weight eleven pounds and 1 ounce, age, fourteen months.

Raffael De M. was admitted to the hospital November 12, 1918, aged six months. He had had chicken-pox and after recovery his general condition remained very poor, with evidences of extreme malnutrition. On January 1, 1919, he was placed on a formula of 30 ounces top milk, 8 ounces of 6 per cent. dextrinized barley gruel, 1.5 ounces lime water and 30 grains of sodium citrate. In addition to his formula he received a cereal and a milk and egg mixture consisting of 1 egg, 200 c.c. milk, 1 gm. salt and 2.5 gm. sugar. The child weighed 14 pounds and 3 ounces on January 7, 13 pounds and 1 ounce on February 28 and 11 pounds and 1 ounce on March 22, when the experiment began; age, 10.3 months.

Michael S. was admitted March 10, 1919, aged eighteen months. He appeared languid and his general condition was fair, while poorly developed. A diagnosis of acute pharyngitis and marasmus was made. On March 12 the child could not retain food, but very gradually his condition improved, so that by March 22 he was retaining all of his diet of bread, butter and milk and egg mixture similar to that of Paul P. On March 19, at the beginning of the experiment, the child weighed 14 pounds and 6 ounces; age 18.3 months. It will be noted that the caloric value of the diets of these children was at no time below the theoretical needs.

At the conclusion of the experiment all four children showed definite improvement, as a result of the addition of vitamins to their diet, while the last two showed such marked improvement that they could be classed as normal children in all respects.

Part B.—John C. was admitted to the hospital April 23, 1919, aged 2.75 months. His general condition was very poor and

his muscles were poorly developed; a diagnosis of marasmus was made. At the beginning of the experiment, June 14, the child weighed 7 pounds and 15 ounces; age, 4.5 months. At the end of the experiment a general improvement was noticed, his musculature and fat were fair, colon and abdomen were somewhat distended and moderate clinical anemia was noted.

Helen B. was admitted to the hospital March 24, 1919, aged six months. Her general condition and musculature were poor. A diagnosis of rickets, marasmus and chronic intestinal dyspepsia was made. Her weight at the beginning of the experiment was 9 pounds and 7 ounces; age, 8.25 months. At the end of the experiment the diagnosis was as follows: Musculature fair, fat fair, abdomen moderately distended, colon distended, digestion better as shown by the stool, and general condition much improved.

Annie de V. was admitted to the hospital January 29, 1919, aged 3.25 months. Her general condition was poor, with little fat and flabby muscles. A diagnosis of rickets, extreme malnutrition, marasmus and bronchitis was made. Her weight at the beginning of the experiment, June 4, was 8 pounds and 4 ounces; age, 7.5 months. At the end of the experiment, although the bronchitis still persisted, the general condition had markedly improved, with fair musculature and fat; abdomen and colon were moderately distended.

Walter McK. was born in the hospital September 11, 1918. He did not nurse well and was put on a formula. He appeared anemic, poorly developed and weighed 11 pounds and 9 ounces at the beginning of the experiment, June 1, when he was 8.66 months old. At the end of the experiment his condition had markedly improved, musculature and fat were good and there was no anemia apparent. He appeared normal in every way.

John P. was admitted to the hospital June 23, 1919, aged eleven months. A diagnosis of bronchitis, marasmus and chronic catarrhal enteritis was made, the general condition being poor. At the beginning of the experiment, July 1, he weighed 14 pounds and 11 ounces. At the end of the experiment the baby appeared very anemic and poorly nourished. A diagnosis of intestinal catarrh was made, it having been evident all along that we were dealing with a sick baby.

John R. was admitted to the hospital March 3, 1919, aged 1.5 months. His general condition was poor and his muscles were poorly developed. A diagnosis of malnutrition was made. The child weighed 9 pounds and 13 ounces at the beginning of the experiment, June 3, when he was 4.5 months old. At the end of the experiment his condition had improved, his musculature and fat were fair, while clinical anemia was observed.

John W. was admitted to the hospital November 15, 1918, aged one month. A diagnosis of gonorrhoeal ophthalmia was made.

His general condition was normal and he appeared to be well nourished. He weighed 11 pounds and 14 ounces at the beginning of the experiment, June 12, when he was eight months old. At the end of the experiment his musculature was good and fat was fair. His general condition was good, though showing clinical anemia.

Frank M. was admitted to the hospital November 4, 1918, aged fifteen days. He was a premature child. At the beginning of the experiment (June 14) his general condition was good and he weighed 11 pounds and 4 ounces; age, 7.75 months. At the end of the experiment his general condition, musculature and fat were fair.

Herbert W. was admitted to the hospital December 12, 1918, aged two months. The general condition was fair, with poor fat and musculature. A diagnosis of intestinal fermentation and malnutrition was made. At the beginning of the experiment (June 3) the weight was 9 pounds and 9 ounces; age, 7.75 months. At the end of the experiment his general condition was about the same as at the start.

William P. was admitted to the hospital June 23, 1919, aged eleven months. At the beginning of the experiment (June 25) he weighed fifteen pounds. His history is the same as that of his twin brother, John P.

DISCUSSION OF RESULTS.

Part A.—A study of the chemical findings in Tables I to IV reveals some interesting observations. In all cases there were only the faintest traces of calcium in the urine. In this connection Flamini⁷ reported in normal children a calcium output of 0.125 gm. per day in terms of calcium oxide, having ingested 5.5 gm. daily; in rachitic children he found an excretion of 0.05 gm. daily, the intake being 3.4 gm. per day. In our cases the intake of calcium, expressed as oxide, varied between 0.49 gm. and 3.9 gm. daily, and yet no measurable urinary elimination was obtained. In Tables I and III it will be seen that the percentage retention of calcium was less in Period II than in Period I and less in Period III than in Period II. In Table II, a case of rickets, we note a progressive increase in the retention indicating a calcium hunger, as has already been observed in cases of rickets. In Table IV the percentage retention in Period II is increased by only 1 per cent., and then drops below that of Period I, similar to what has been recorded in Tables I and III. Obviously, as the experiment progressed, the need of the body for calcium, except in the case of rickets, became less urgent.

The daily elimination of phosphorus was very small, approximately one-fifth of the normal, on an intake varying from 0.36 gm. to 2.18 gm. per day. In three instances, Tables I to III, the percentage retention of phosphorus was less in Period II than in Period I

and less in Period III than in Period II. In the fourth case (Table IV) the percentage retention was greater in Period II than in Period I and less in Period III than in Period II.

Regarding the metabolism of nitrogen we have in every case, during certain periods, as shown in the tables, the apparent paradox of a retention of nitrogen accompanied by a loss in weight. A similar observation was made by one of us (H. E. D.), working with Schamberg, Kolmer, Ringer and Raiziss, in an investigation of psoriasis.⁸ Observations of this kind were also reported as far back as 1860 by Bischoff and Voit,⁹ and by Lüthje and Berger¹⁰ experimenting with dogs. This retention of nitrogen without a corresponding gain in weight can be accounted for by assuming constantly changing water content of the tissues. Work done in Rubner's laboratory¹¹ has shown that in starvation the relative amounts of water in the tissues may increase quite markedly, at the same time that the relative amount of solid material decreases. While our children were not starving it is, nevertheless, obvious that in their state of extreme undernutrition there is a marked craving for nitrogen, and this craving was being satisfied, as evidenced by the nitrogen retention. It may be seen that all four children showed less retention in Period II than in Period I and still less in Period III than in Period II.

In general, therefore, there was a decreasing percentage retention of calcium, phosphorus and nitrogen, showing a gradual approach toward the normal. Whether or not these findings are directly due to the vitamine feeding we cannot say, although it is reasonable to assume that they are. It is quite possible that further detailed experimentation with vitamine feeding may yield definitely positive chemical findings, but for the present, at least, we must satisfy ourselves with the growth curve as the best evidence of vitamine therapy, and this brings us to an examination of the weight charts.

It is evident from Chart I that the children gained more weight during the vitamine-feeding period than in the fore period. In the after period two continued to gain weight while the remaining two lost 2 ounces each.

Looking at Table V we see that in the fore period of twenty-two days Paul P. gained only 3 ounces, in the vitamine period of twenty-eight days he gained 19 ounces and in the after period of twenty-one days he lost 2 ounces.

William D. in the fore period of nineteen days lost 5 ounces, in the vitamine period he gained 24 ounces and in the after period he lost 2 ounces.

Raffael De M. in the fore period of nineteen days gained 15 ounces, in the vitamine period he gained 62 ounces and in the after period he gained 12 ounces.

Michael S. in the fore period of nineteen days gained 18 ounces, in the vitamine period he gained 68 ounces and in the after period he gained 30 ounces.

It is not unlikely that if the first two children had received vitamine feeding over a longer period of time they would have done as well in the after period as the second two children. There is no doubt, however, that the rate of growth of all four children was greatly increased as a direct result of having received in their usual diet a daily feeding of the vitamine preparation.

Part B.—Having obtained such satisfactory results with these four children, we continued our experiment with ten more children, as already described, keeping a record of the weight changes only. The results obtained are recorded in Charts II and III and summarized in Table VI. At the end of the fore period Lot V received daily doses of vitamins in addition to their usual diet, while Lot C acted as controls.

Taking up Lot V, we see that John C. gained 5 ounces in the fore period of twenty-eight days and 21 ounces in the vitamine period of forty days.

Helen B. gained 9 ounces in the fore period of thirty-eight days and 20 ounces in the vitamine period.

Anna Da V. gained 10 ounces in the ten days fore period and 30 ounces in the vitamine period.

Walter McK. gained 11 ounces in the fore period of thirty-nine days and 48 ounces in the vitamine period.

John P. gained 1 ounce in the fore period of ten days and lost 18 ounces in the vitamine period. More will be said about this baby later.

In Lot C., John R. gained 8 ounces in the thirty-seven days fore period and 20 ounces in the forty days control period. It is, however, worthy of note that during the first ten days of the fore period this child lost 23 ounces while in the remaining twenty-seven days it gained 34 ounces as against only 20 ounces in the next forty days of the control period. In other words the rate of gain in the control period had fallen off considerably from what it had been in the immediately preceding twenty-seven days of the fore period.

John W. gained 3 ounces in the fore period of thirty days and only 7 ounces in the control period.

Frank M. gained 7 ounces in the fore period of twenty-eight days against 4 ounces in the control period.

Herbert W. gained 16 ounces in the fore period of thirty-eight days and only 4 ounces in the control period.

William P. gained 5 ounces in the fore period of sixteen days and lost 7 ounces in the control period. This baby and John P. of Lot V, are twin brothers, and were found to be suffering from intestinal catarrh. They may therefore be ruled out in the conclusions to be drawn from the results obtained.

It is quite clear in this part of the experiment, just as in Part A, that those children who received daily doses of the vitamine preparation in addition to their usual diet gained weight much more rapidly than those to whom vitamins were not given. At the end of the experiment

the general condition of the children who had received the vitamine product was somewhat better than that of the children who had acted as controls.

VITAMINES IN RELATION TO GROWTH.

Funk,¹² Harden and Zilva,¹³ Drummond¹⁴ and many other investigators have shown that growth takes place best when the diet includes the antiscorbutic, the antineuritic and the antirachitic vitamins, thus affording what might be termed a "*diet of sufficiency.*" It does not matter, from a practical point of view, whether we accept the above vitamine classification or the "fat-soluble A, water-soluble B" classification. Nor does it matter whether we call them "vitamines" or "food accessories," from a practical standpoint. The prime factor is that those substances of whose chemical composition we are still in the dark are admittedly necessary for proper growth.

Theoretically, however, we prefer the term "vitamine" to "food accessory," because a substance which is so vitally necessary for growth and for life itself can hardly be called an "accessory." Regarding the "fat-soluble A, water-soluble B, water-soluble C" classification of Drummond,¹⁴ as opposed to the "antirachitic, antineuritic, antiscorbutic vitamins" classification, we believe that the latter is the more accurate. Drummond¹⁵ supports the view that the antineuritic vitamine and the water-soluble growth accessory factor are either identical or else individually closely related members of the same class. While it is true that the antirachitic vitamine is found in certain fats and oils, it is also true that the supposedly "water-soluble B" may be dissolved in olive oil, as Myers¹⁶ has demonstrated, and might therefore also be termed "fat-soluble."

The probability that antirachitic vitamine is either identical with "fat-soluble A" or has a somewhat similar distribution to "fat-soluble A" is discussed by Mellanby¹⁷ in his paper "An Experimental Investigation on Rickets." Using dogs, he found that the animal fats were more antirachitic than the vegetable fats. The best of the vegetable fats are arachis (peanut) and olive oils; the worst of those examined include linseed, cottonseed, babassu oils, a hydrogenated fat and coconut oil. In other words the antirachitic substances for the most part were found to be similar to those in which, according to the experiments on growth of McCollum, Osborne and Mendel and others, "fat-soluble A" is present. From the results of his experiments, and a consideration of the growth experiments on rats, of other investigators, Mellanby concludes that, on the whole, the antirachitic vitamine and fat-soluble A appear to be identical. As to the relationship between the antineuritic and antiscorbutic vitamins, Harden and Zilva¹⁸ and others have concluded that they are not identical, since substances showing marked antineuritic activity are antiscorbutically inactive, and *vice versa*.

McCullum's contention that scurvy is of intestinal origin has been disproved by many investigators. Givens, Hart, Hess, Mendel, Steenbock and their co-workers in this country and Chick, Hume and Skelton, Harden and Zilva and others in England have all substantiated the earlier view of Funk⁴ that the disease is the result of a deficiency of some nutritive factor in the diet. In a recent personal communication to Chick,* McCullum has abandoned his early view on scurvy in favor of the generally accepted opinion that it is a "deficiency disease." We may therefore consider the antiscorbutic vitamin as distinct from the antirachitic vitamin associated with rickets and from the antineuritic vitamin associated with beriberi and polyneuritis. Hopkins¹⁹ is likewise of the opinion that there are three distinctive vitamins, as just enumerated, and that each is concerned with a definite nutritional disturbance. *It may indeed ultimately develop that other nutritional disturbances or "deficiency diseases" are each associated with a distinct and separate vitamin.*

The relation of the vitamins to growth is again shown by the work of Kligler²⁰ in demonstrating that the growth of various pathogenic bacteria studied was favorably influenced by the addition of small amounts of watery extracts of various tissues; the ether extracts had no effect on growth; experiments are reported which indicate that the substance responsible for growth belongs to the class of so-called vitamins. This work is quoted merely to show the value of the watery extract as against the ether extract.

Another observation of a somewhat similar character is that of Emmet and Allen,²¹ who found in experiments on the growth of tadpoles that too much fat in the diet was injurious to growth. The lack of vitamin obtained from yeast was more apparent than that obtained from fat, and in the absence of vitamins, growth and development were distinctly retarded.

Hess,²² using liquid autolyzed yeast, found that it was an excellent stimulant to growth. It also exerted a favorable effect on the digestive processes as evidenced not only by a gain in weight and increased appetite, but also by the character of the stools. These findings are corroborated by ours in every particular, emphasizing the fact that the vitamin preparation retained the activity of the fresh autolyzed yeast.

Drummond²³ noted that an increase in food intake could be brought about by adding flavoring extracts, such as meat extract, to the diet, but unless the additions contain vitamin no growth results. Such facts make it apparent that vitamins are more than mere "appetizers," and that any increase in appetite would be more likely due to the improved condition of the individual, owing to the presence of vitamin in the diet. The results of our experiments lead us to believe that the water-soluble or antineuritic vitamin,

* Jour. Biol. Chem., 1919, xxxix, 204.

as we prefer to call it, supplies some essential factor which makes growth possible, since a mere increase in appetite does not result in an increase in weight if the added food is not properly assimilated.

Bearing upon the supply of antineuritic vitamin in the diet of the infant, an editorial in the *Journal of the American Medical Association*²⁴ says: "As Osborne and Mendel point out, the practice of reinforcing the supply of calories by diluting top milk and adding lactose leads to difficulties. Here the child is supplied with a food that contains a relatively smaller proportion of the water-soluble vitamin than does the original cow's milk. While this may contain enough vitamin as long as the intake is normal, if for any reason the child's appetite fails, the vitamin supply is reduced and various dietary troubles may easily result. This vitamin is of particular importance beyond the earlier stages of development, when to a scanty allowance of milk are added various foods poor in vitamins, thus giving rise to disorders."

Funk¹² and also Drummond¹⁵ have shown that satisfactory growth has been secured with antineuritic vitamin in the absence of antirachitic vitamin, but the reverse is not true, which shows that the antineuritic vitamin is of greater importance than the antirachitic. Deprivation of the latter is not felt as soon as removal of the former, since in its own fat stores the body possesses a supply of the antirachitic vitamin, which it appears able to call upon when necessary. Funk¹⁴ is of the opinion that the antineuritic vitamin is the only vitamin concerned with actual growth, while the antirachitic and antiscorbutic vitamins are specific for rickets and scurvy. This conception seems to be borne out by the numerous experiments of Mellanby, McCollum, Hess, Drummond and others, which show that in the absence of antineuritic vitamin proper growth does not take place even though the antirachitic and antiscorbutic vitamins are present.

On the other hand, Hess²² showed that scurvy may develop, accompanied by an increase of weight. Likewise, Mellanby¹⁷ demonstrated that rickets develops most easily in the fastest growing dogs. Both the scurvy and rickets could be cured by the administration of the respective vitamins, but no growth would occur unless the antineuritic vitamin was present in the diet. *We are therefore led to the inevitable conclusion that while the antineuritic vitamin is most important for growth, special care should be taken to see that the needs of the body for the three known vitamins are supplied, in order that adequate growth and general well-being may be obtained.**

In a recent paper Drummond²⁵ shows that although the fat-

* In a late publication (*Am. Jour. Dis. Children*), abstracted in this issue, Daniels, Byfield and Loughlin demonstrate that antineuritic vitamin added to the diet of babies supplied with food furnishing an adequate number of calories stimulates growth. This corroborates our findings and supports us in our assertion that the antineuritic vitamin is the one chiefly concerned with growth, although all of the three known vitamins are essential to complete growth and general well-being.

soluble or antirachitic vitamine is not strictly a growth factor, it is necessary for the maintenance of health in the adult rat. It is also necessary for the female rat during pregnancy and lactation. The absence of this factor brings about a lowering of resistance to diseases of bacterial origin, and consequently great care must be taken to ensure that dietaries of adults contain an adequate supply of this vitamine.

The statement just made takes on added significance in the light of the recently reported experiments of Bulley,²⁶ which tend to show that "xerophthalmia," an infection of the eye, is not a "deficiency disease," as has been held by McCollum, Simmonds and Pitz,²⁷ who said, "xerophthalmia and polyneuritis are abundantly demonstrated to have their origin in the lack of a sufficient amount of the fat-soluble A and water-soluble B growth accessory factors respectively." It may not be amiss to give in some detail the observations of Bulley,²⁶ and we shall do so as nearly as possible in her own words:

"That eye symptoms in rats may occur as a result of deficiencies in the diet seems to be a common experience. It is very important, however, to distinguish between symptoms due directly to a specific dietetic error and any that may be due to infection, encouraged, it may be, by diminished resistance due to the diet. My own experience seems to point to the fact that so far as xerophthalmia is concerned the latter relation is the true one. Since January, 1918, to date, 500 young rats were kept on various experimental diets. About half of the animals received fat-soluble A in the diet while the other half were given diets in which fat-soluble A was either absent or deficient. The basal diet consisted of extracted caseinogen, unextracted starch, sugar and salts. The stock animals from which the experimental animals were taken were fed on bread, milk, oats and various vegetables. To all the diets there was added a fat-free alcoholic extract of a yeast preparation.

"Of all the animals used only five showed xerophthalmia. Two occurred on a diet containing fat-soluble A to a limited extent; 1, where fat-soluble A was present in presumably sufficient quantities; 1 on an ample stock diet; and 1, where fat-soluble A was probably absent. Each experiment lasted three or four months, and in each experiment there were at least eight other animals on the respective diets, showing no symptoms of xerophthalmia at all. On this evidence, xerophthalmia would appear to have no direct relation to diet, since these 5 cases were on different types of food and to have little relation to growth.

"These results are attributed to the fact that (a) no trouble has been spared to keep the animals under the very cleanest and healthiest conditions, and (b) care has always been taken to treat very promptly with boracic lotion all cases of slightly sore-looking eyes. Regarding the clearing up of symptoms of xerophthalmia observed by others on giving fat-soluble A it is likely that as in so

many cases of obstinate infection general improvement of health brings about a cure of local condition. With avoidance of initial infection animals can be kept almost entirely free of this so-called "deficiency disease" whether fat-soluble A be present or absent. It is dangerous to draw conclusions as to the presence or absence of fat-soluble A in any diet merely from the appearance of xerophthalmia."

Funk¹² has obtained eye symptoms in rats even while their diet contained butter. These symptoms could be cleared up by washing the eyes with zinc sulphate solution, and also by adding antineuritic vitamine to the diet. This would seem to indicate that the sore eye condition is due to poor nutrition and not to a dietary deficiency.

It is evident from the foregoing statements that doubt is cast upon the belief that xerophthalmia is, in the true sense, a deficiency disease, so that the original classification of Funk⁴ still holds good, at least as regards beriberi, scurvy and rickets.

Hart²⁸ and his co-workers showed that milk sterilized at 120° C. for ten minutes, commercial unsweetened condensed milk and commercial milk powder (Merrei-Soule) had lost their antiscorbutic properties when used in quantities equivalent to an amount of raw milk which would prevent scurvy in guinea-pigs on a diet of rolled oats and dried hay. The growth-promoting properties, however, are unaffected by the drying of milk. This emphasizes the importance of the use of some antiscorbutic in conjunction with infant-feeding. Hess²⁹ advocates the use of antiscorbutics in infant-feeding even as early as at the end of the first month of life. Orange-juice or lemon-juice may be used, but some stable antiscorbutic should be available for clinical use in view of the irregularity with which the various natural antiscorbutic products come into the market and the uncertain prices. Similarly, vegetable margarine should not be used exclusively because of the necessity of antirachitic vitamine in teeth-formation. Hume and Skeleton³⁰ show that a diet containing the antirachitic vitamine, as in butter, allows the development of sound teeth in puppies. In this connection Fisher³¹ points out that delayed teething is undoubtedly due to insufficient phosphorus and vitamins in the food.

In concluding this brief discussion we would suggest that the "antirachitic, antineuritic and antiscorbutic" classification of the vitamins be used as being best descriptive of the three definitely established "deficiency diseases"—rickets, beriberi and scurvy.

PREPARATION OF THE VITAMINE PRODUCT.

The vitamine product "V" is prepared from corn, antolyzed yeast and orange-juice, thereby assuring the presence of antineuritic, antirachitic and antiscorbutic vitamins. The final product is dried

in vacuo at a low temperature, thus avoiding the destruction of the vitamins, particularly the antiscorbutic, which is the most unstable. In this connection, Harden and Robinson³² report that by drying orange-juice *in vacuo* at 40° C. it is possible to obtain a solid residue possessing, in a high degree, the antiscorbutic property of the fresh juice. This value is not appreciably diminished when the substance is kept in a dry atmosphere at room temperature for six months. The stability of the antineuritic and antirachitic vitamins has been amply demonstrated by Funk,¹ McCollum and Davis,³³ Osborne and Mendel³⁴ and others.

Some doubt, however, has been thrown on the supposed stability of the antirachitic vitamin. Steenbock, Boutwell and Kent³⁵ have shown that the exposure of butter fat to 100° C. for four hours destroys almost completely the antirachitic vitamin. Drummond,³⁶ using butter fat and whale oil, shows that a temperature of 100° C. for one hour gives the same results. From the results of his experiments he advances somewhat hesitatingly the hypothesis that "fat-soluble A is not a clearly defined chemical substance, but rather that it is a labile substance, perhaps possessing characteristics resembling those of an enzyme." Owing to these conflicting views it is obvious that further work will have to be done to establish the validity of one or the other. *Nevertheless, it has been demonstrated that low temperatures, for example, from 40° to 50° C., have no deleterious influence on the activity of the vitamins.*

The vitamin preparation is a grayish-white powder, practically odorless, slightly sweet when prepared for ingestion and devoid of toxic properties. It is stable, non-hygroscopic, sparingly soluble in water and strong organic acids, much more soluble in dilute acids and gastric juice and practically completely soluble in concentrated mineral acids. The activity of the vitamin product has been unchanged during five months, and because of the method of preparation it will undoubtedly retain its activity for longer periods of time. It may be mentioned here that properly dried yeast has up to date retained its activity for three years.¹⁶ It has been thought advisable to store the vitamin product in the dark to avoid any possible deleterious action of light. Regarding this precaution, Zilva³⁷ has found that butter exposed for eight hours to ultraviolet light undergoes very noticeable changes and loses its antirachitic value. However, similar experiments with the antineuritic vitamin of yeast and the antiscorbutic vitamin of lemon-juice shows that neither one loses its activity. As shown by Funk,³³ radium emanations have no effect on the activity of autolyzed yeast, which contains both antineuritic and antirachitic vitamins.

A tentative analysis of the vitamin product shows the following chief constituents: Calcium, expressed as calcium oxide, 10 per cent.; phosphorus, 15 per cent.; nitrogen, 3.5 per cent.; fat, 2.5

per cent.; iron, 0.3 per cent.; silicates, 5.6 per cent.; moisture, 10 per cent.; the remainder is made up of the rest of the phytin molecule—of which the vitamine preparation is chiefly constituted—which is a double calcium and magnesium salt of inosite pentaphosphoric acid. *The value of the preparation, however, lies largely in its vitamine content. As for the calcium and phosphorus present, although it is impossible to attribute to them any definite therapeutic value, it is admitted that both are important in the diet, presumably for the purpose of bone and tooth formation.*³¹

As we go to press our attention is called to an editorial³⁹ entitled "Do Americans Need More Calcium?" The editorial goes on to say:

"Sherman⁴⁰ has come to the conclusion that 'ordinary mixed diet of Americans and Europeans, at least among dwellers in cities and towns, is probably more often deficient in calcium than in any other chemical element.' In the case of the growing individual lime must be provided for the normal development of the bones, which include 99 per cent. of this element. The pregnant mother needs calcium for the rapid increment of the fetus, and during lactation she has a similar requirement for the production of a secretion, milk, which is exceptionally rich in it. The tendency toward a shortage of calcium is not confined to the human species. Forbes⁴¹ has shown this to be true in the cow. The average daily calcium requirement has been estimated as a little less than 0.5 gm. per man. It is proposed by McCollum and his collaborators⁴² that an addition of calcium could be most conveniently made to our foods through the use of a mixture of equal parts of common salt and calcium carbonate in the kitchen and on the table. This suggestion deserves a sympathetic hearing."

Mellanby¹⁷ makes the point that "it is more than probable that a deficient calcium intake associated with deficient antirachitic factor will bring about a more acute production of rickets and must always be an adjuvant factor to be considered in the etiology of rickets."

In view of the foregoing, and judging from the findings recorded in Tables I to IV, it must be concluded that the presence of both calcium and phosphorus in the vitamine preparation is a distinct advantage.

SUMMARY.

We have prepared a stable vitamine product, briefly designated, "V." An analysis shows the chief components to be calcium, expressed as calcium oxide, 10 per cent.; phosphorus, 15 per cent.; nitrogen, 3.5 per cent.; fat, 2.5 per cent.; iron, 0.3 per cent.; silicates, 5.6 per cent.; moisture, 10 per cent. The remainder goes to make up the rest of the phytin molecule—the main constituent of the product—which is a double calcium and magnesium compound of inosite phosphoric acid.

Owing to the method of preparation and to the results of our experiments with normal and polyneuritic pigeons, normal and scorbutic guinea-pigs and finally with children presenting evidence of malnutrition, marasmus and rickets—a marked acceleration in the rate of growth having been obtained, particularly in the children—it is established that the product contains antineuritic, antiscorbutic and antirachitic vitamins. The calcium and phosphorus present in the product undoubtedly have a beneficial action on the general metabolism, more particularly perhaps on bone- and tooth-formation.

The pigeon and guinea-pig experiments demonstrate directly the presence of antineuritic and antiscorbutic vitamins. Regarding the latter, guinea-pigs getting the vitamin preparation have been kept free from scurvy for from forty-four to fifty-five days thus far while on a scurvy-producing diet of hay, oats and autoclaved milk. These results will be published at an early date upon the completion of the experiments. As for the antirachitic vitamin, although we know that it is present as explained earlier in this summary we intend to further demonstrate its presence by experiments similar to those of Mellanby.¹⁷

It is felt that until such time as the vitamins shall have been isolated and their chemical composition determined the vitamin preparation which we have produced is an admirable substitute and may be used with confidence in just such a manner as described by Voegtlin.⁵ It is not intended as a substitute for any method of treatment nor is it meant to be used in infant feeding only. Rather is it intended to be a valuable aid whenever its use is indicated. At the same time it should not be lost sight of that the diet must contain sufficient protein, fats, carbohydrates and mineral salts and that the caloric value must be adequate for the needs of the individual.

It may be stated here that it is shortly planned to start an extended investigation, with the hope of isolating and determining the chemical composition of the vitamins.

We wish to express our appreciation of the valuable assistance given us by Mr. B. Shapiro in the laboratory throughout the entire experiment.

The authors wish to make acknowledgement of the coöperation accorded them by the staff of the Metropolitan Hospital. Dr. Walter Conley, superintendent of the institution; Dr. Benson, chief of the children's division; Dr. Bingham, orthopedist; Dr. Simonson, pediatricist, by whom the formulas were written, and his assistant, Dr. Vokes, and Dr. McHugh, of the house staff, seriously interested themselves in all of the work being done at the bedside, while Dr. Larkin and Dr. Hiss placed their counsel and every laboratory facility at our disposal. Our appreciation of the generous and helpful advice and assistance of those mentioned is herewith gladly and properly made a part of this contribution to a study of the vitamins.

TABLE I.—PAUL P.

Period.	Day ending 1919.	Ingestion.			Excretion.			Balance.			Retention.			Wt. gain or loss, oz.				
		N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., per cent.	CaO., per cent.	P., per cent.					
I	Mar. 29	4.641	0.998	0.633	2.200	trace	0.145	2.351	0.815	0.420	57.3	85.0	74.5	-2				
	30	6.408	1.341	0.936	2.250	"	0.142	4.068	1.158	0.726								
	31	5.794	1.235	0.797	2.330	"	0.143	3.374	1.052	0.586								
	Apr. 1	6.202	1.293	0.576	2.530	"	0.153	3.582	1.110	0.655								
	2	6.389	1.298	0.930	2.270	"	0.162	4.029	1.115	0.700								
	3	6.164	1.212	0.865	2.620	"	0.167	3.454	1.029	0.630								
	4	6.336	1.350	0.974	3.400	"	0.163	2.846	1.157	0.743								
	5	6.274	1.380	0.858	2.210	"	0.142	3.974	1.197	0.648								
	Feces	0.760	1.470	0.544
	Total	..	18.208	10.107	6.869	20.760	1.470	1.761	27.638	8.637					5.108
II*	May 3	6.802	1.634	1.230	3.200	trace	0.199	3.247	1.256	0.890	46.5	79.3	73.2	+7				
	4	7.364	1.779	1.307	3.240	"	0.193	3.769	1.401	0.973								
	5	7.145	1.738	1.267	3.140	"	0.206	3.610	1.360	0.920								
	6	8.335	2.053	1.434	3.870	"	0.219	4.110	1.675	1.074								
	7	7.769	1.962	1.363	4.310	"	0.246	3.104	1.584	0.976								
	8	7.509	1.795	1.361	4.100	"	0.213	3.054	1.417	1.008								
	Feces	2.130	2.270	0.850
	Total	..	44.924	10.961	7.963	24.030	2.270	2.126	20.894	8.691					5.837
III	May 24	7.070	1.686	1.103	3.790	trace	0.262	3.154	1.360	0.729	29.6	75.6	61.7	+4				
	25	6.163	1.418	0.969	4.070	"	0.245	1.967	1.092	0.612								
	26	4.859	1.101	0.766	3.870	"	0.229	0.863	0.775	0.425								
	27	5.938	1.368	0.937	4.640	"	0.271	1.172	1.042	0.554								
	28	5.682	1.344	0.871	3.920	"	0.217	1.636	1.018	0.542								
	Feces	0.630	1.630	0.560
Total	..	29.712	6.917	4.616	20.920	1.630	1.784	8.792	5.287	2.862				

In this period, one gram of the vitamine preparation was fed daily.

TABLE II.—WILLIAM D.

Period.	Day ending 1919.	Ingestion.			Excretion.			Balance. +			Retention.			Wt. gain or loss, oz.				
		N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., per cent.	CaO., per cent.	P., per cent.					
I	Mar. 29	5.750	1.920	1.065	2.980	trace	0.175	2.341	1.170	0.778	40.5	67.0	73.8	-4				
	30	6.070	2.028	1.125	3.270	"	0.177	2.371	1.478	0.836								
	31	6.810	2.270	1.260	3.000	"	0.162	3.381	1.620	0.986								
	April 1	5.520	1.840	1.020	3.110	"	0.170	1.981	1.190	0.738								
	2	5.270	1.757	0.975	2.830	"	0.158	2.011	1.107	0.705								
	3	5.830	1.945	1.080	2.860	"	0.155	2.541	1.295	0.813								
	4	4.910	1.650	0.915	2.870	"	0.170	1.641	1.000	0.633								
	5	5.830	1.945	1.080	2.990	"	0.172	2.411	1.295	0.796								
	Feces	3.430	5.200	0.900
	Total	..	46.920	15.755	8.520	27.340	5.200	2.239	18.680	10.555					6.281
II*	May 3	7.110	2.127	1.450	3.510	trace	0.284	2.930	1.664	1.018	34.0	70.9	69.6	+0				
	4	7.490	2.555	1.450	3.690	"	0.288	3.130	1.792	1.014								
	5	7.800	2.662	1.580	3.710	"	0.309	3.420	1.899	1.123								
	6	7.800	2.662	1.580	4.900	"	0.382	2.230	1.899	1.050								
	7	7.160	2.447	1.460	4.590	"	0.356	1.900	1.784	0.954								
	8	8.630	2.932	1.730	4.640	"	0.331	2.320	2.169	1.251								
	Feces	4.020	4.580	0.890
	Total	..	15.990	15.685	9.320	29.060	4.580	2.840	16.930	11.105					6.480
III	May 24	8.420	2.810	1.560	3.290	trace	0.240	4.902	2.234	1.198	37.0	73.0	65.0	+2				
	25	5.830	1.945	1.080	3.620	"	0.294	1.982	1.369	0.564								
	26	5.830	1.945	1.080	3.660	"	0.292	1.942	1.369	0.666								
	27	5.520	1.840	1.020	3.830	"	0.288	1.462	1.261	0.610								
	28	6.320	2.110	1.070	4.580	"	0.341	1.512	1.531	0.607								
	Feces	1.140	2.880	0.610
Total	..	31.920	10.650	5.910	20.120	2.880	2.065	11.800	7.770	3.845				

In this period, one gram of the vitamine preparation was fed daily.

TABLE III.—RAFFAEL DE M.

Period	Day ending 1919.	Ingestion.			Excretion.			Balance.			Retention.			Wt. gain or loss, oz.
		N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., per cent.	CaO., per cent.	P., per cent.	
I	Mar. 29	7.026	3.731	1.949	3.740	trace	0.238	3.071	2.959	1.489				
	30	7.021	3.765	2.017	4.660	"	0.288	2.146	2.993	1.507				
	31	7.021	3.765	2.017	3.050	"	0.195	3.746	2.993	1.600				
	April 1	7.021	3.765	2.017	3.070	"	0.345	3.736	2.993	1.450				
	2	6.916	3.650	1.959	3.370	"	0.210	3.331	2.878	1.527				
	3	7.156	3.810	2.042	3.730	"	0.249	3.211	3.038	1.571	44.4	79.2	76.0	+8
	4	7.156	3.810	2.042	4.020	"	0.310	2.921	3.038	1.510				
	5	7.156	3.810	2.042	4.050	"	0.250	2.891	3.038	1.570				
	Feces	1.720	6.180	1.780							
	Total		56.473	30.096	16.085	31.420	6.180	3.865	25.053	23.916	12.220			
II*	May 3	7.132	3.877	2.181	4.340	trace	0.265	2.401	2.697	1.671				
	4	7.132	3.877	2.181	4.780	"	0.286	1.961	2.697	1.650				
	5	7.132	3.877	2.181	4.550	"	0.306	2.191	2.697	1.630				
	6	7.132	3.877	2.181	5.010	"	0.312	1.731	2.697	1.624				
	7	7.132	3.877	2.181	4.910	"	0.286	1.831	2.697	1.650	27.5	69.5	75.0	-2
	8	7.132	3.877	2.181	5.080	"	0.341	1.661	2.697	1.595				
	Feces	2.350	7.080	1.470							
	Total		42.792	23.262	13.086	31.020	7.080	3.266	11.772	16.182	9.820			
III	May 24	7.462	3.850	2.075	6.580	trace	0.401	0.451	1.682	1.334				
	25	7.437	3.874	2.085	4.430	"	0.303	2.577	1.706	1.442				
	26	7.522	3.890	2.096	5.970	"	0.373	1.122	1.722	1.383				
	27	7.622	3.424	1.873	5.900	"	0.377	1.292	1.256	1.156				
	28	7.599	3.602	1.957	5.950	"	0.392	1.219	1.434	1.225	17.6	49.9	64.9	-5
	Feces	2.150	10.840	1.700							
Total		37.642	21.640	10.086	30.980	10.840	3.546	6.662	10.800	6.540				

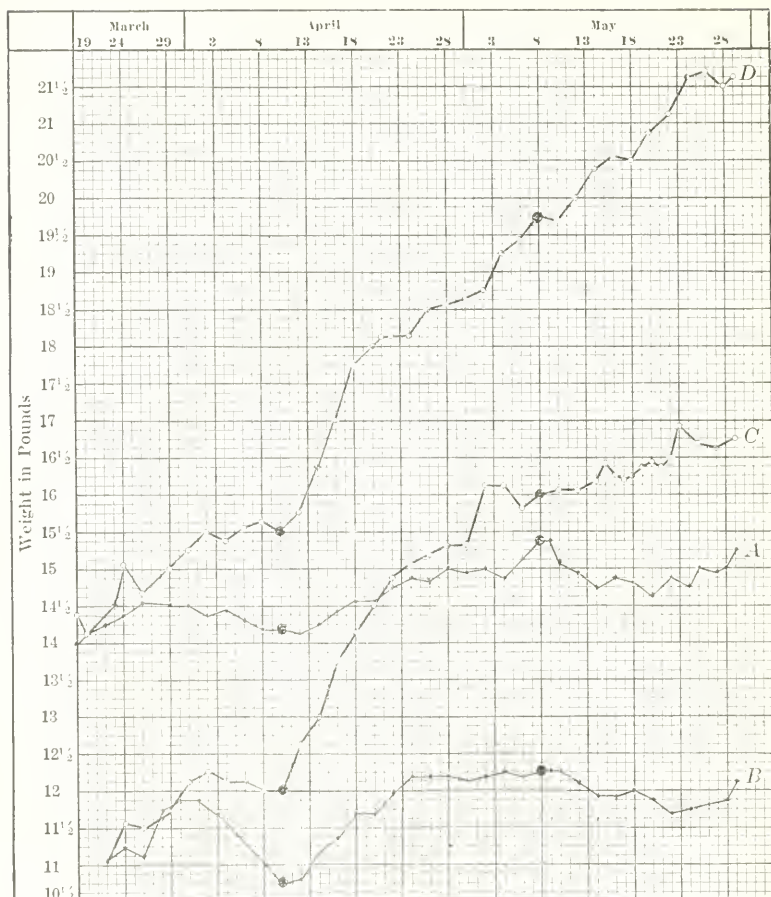
In this period, one gram of the vitamine preparation was fed daily.

TABLE IV.—MICHAEL S.

Period	Day ending 1919.	Ingestion.			Excretion.			Balance. +			Retention.			Wt. gain or loss, oz.
		N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., gm.	CaO., gm.	P., gm.	N., per cent.	CaO., per cent.	P., per cent.	
I	Mar. 29	2.150	0.815	0.498	1.340	trace	0.057	0.598	0.442	0.318				
	30	1.794	0.490	0.361	1.400	"	0.050	0.182	0.117	0.188				
	31	2.204	0.614	0.449	1.480	"	0.059	0.512	0.241	0.267				
	April 1	3.583	0.964	0.740	1.460	"	0.061	1.911	0.591	0.566				
	2	4.734	1.155	1.018	1.950	"	0.071	2.572	0.782	0.824				
	3	4.983	1.115	1.106	1.830	"	0.074	2.941	0.742	0.909	47.1	59.5	75.5	+6
	4	4.641	1.112	1.007	1.990	"	0.086	2.439	0.739	0.798				
	5	4.797	1.116	1.049	2.140	"	0.081	2.445	0.743	0.845				
Feces	1.700	2.990	0.990								
Total		28.886	7.381	6.228	15.290	2.990	1.529	13.596	4.391	4.699				
II*	May 3	6.584	1.223	1.702	2.810	trace	0.149	3.274	0.743	1.450				
	4	6.719	1.229	1.747	2.910	"	0.164	3.309	0.749	1.480				
	5	6.462	1.223	1.665	2.980	"	0.187	2.982	0.743	1.375				
	6	6.491	1.222	1.674	3.740	"	0.218	2.251	0.742	1.353				
	7	6.147	1.170	1.589	3.490	"	0.249	2.157	0.690	1.337	42.3	60.5	82.2	+12
	8	6.667	1.227	1.723	3.620	"	0.201	2.547	0.747	1.419				
	Feces	3.000	2.880	0.620							
	Total		39.070	7.294	10.100	22.550	2.880	1.788	16.520	4.414	9.312			
III	May 24	6.578	1.156	1.569	3.480	trace	0.185	2.916	0.662	1.296				
	25	6.413	1.152	1.521	5.440	"	0.336	0.791	0.658	1.097				
	26	6.608	1.156	1.577	4.490	"	0.239	1.936	0.662	1.250				
	27	6.481	1.153	1.541	2.990	"	0.144	3.309	0.659	1.309				
	28	6.570	1.155	1.567	4.240	"	0.228	2.148	0.661	1.251	34.0	57.2	79.8	-2
	Feces	0.910	2.470	0.439							
Total		32.650	5.772	7.775	21.550	2.470	1.571	11.100	3.302	6.204				

In this period, one gram of the vitamine preparation was fed daily.

CHART 1.



- A. Paul P., 19.0 months old at start of experiment.
 B. William D., 14.0 " " " " "
 C. Raffael DeM., 10.3 " " " " "
 D. Michael S., 18.3 " " " " "

● Feeding of vitamin preparation from April 10 to May 8, 1 gram per day.

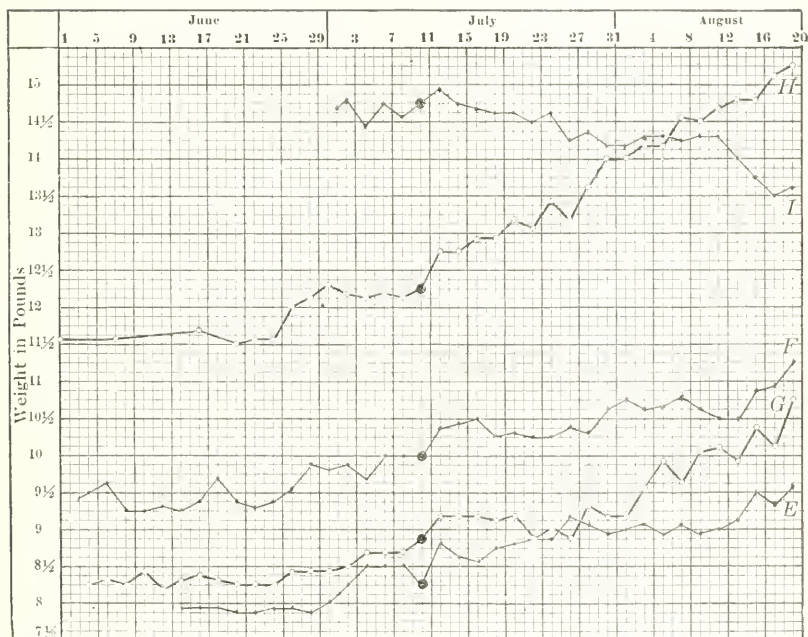
TABLE V.

PATIENT	FORE PERIOD	VITAMINE PERIOD	AFTER PERIOD
	I OUNCES 3/19-4/10=22 days	II OUNCES 4/10-5/8=28 days	III OUNCES 5/8-5/29=21 days
Paul F.	+ 3	+19	- 2
Wm. D.	- 5	+24	- 2
Raffael DeM.	+15	+62	+12
Michael S.	+18	+68	+30

* Controls, no vitamine given.

† Twin brothers, ruled out of the experiment because of chronic catarrhal enteritis.

CHART II.



E. John C., 4.5 months old at start of experiment.

F. Helen B., 8.25 " " " " " "

G. Anna DaV., 7.5 " " " " " "

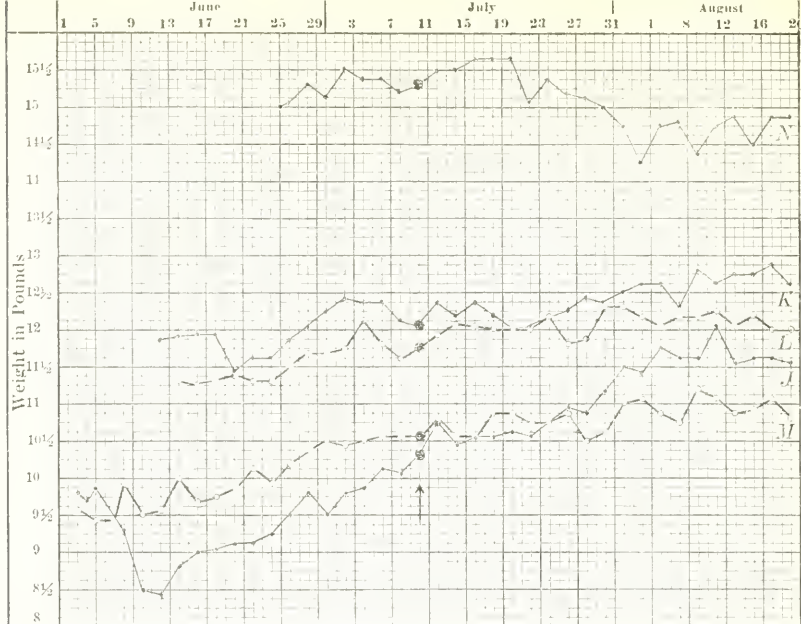
H. Walter McK., 8.66 " " " " " "

I. John P., 11.00 " " " " " "

This baby was ruled out

of experiment because of chronic catarrhal enteritis

● Feeding of vitamine preparation from July 10 to end of experiment, 1 gram daily until August 12 and 2 grams daily thereafter.



- J. John R., 4.5 months old at start of experiment.
 K. John W., 8.0 " " " " "
 L. Frank M., 7.75 " " " " "
 M. Herbert W., 7.75 " " " " "
 N. William P., 11.00 " " " " " Twin brother of John P.
 also ruled out of experiment because of chronic catarrhal enteritis.

† Beginning of period for comparison with vitamine-fed babies.

TABLE VI.

PATIENT	FORE PERIOD	VITAMINE PERIOD
	I OUNCES	II OUNCES
John C.	6/11-7/10=26 days + 5	7/10-8/19=10 days +21
Helen B.	6/3-7/10=37 days + 9	+20
Anna DaV.	6/4-7/10=36 days +10	+30
Walter McK.	6/1-7/10=39 days +11	+48
John P. †	7/1-7/10= 9 days + 1	-18
LOT C.*	6/3-7/10=37 days	
John R.	+ 8	+20
John W.	6/12-7/10=28 days + 3	+ 7
Frank M.	6/14-7/10=26 days + 7	+ 4
Herbert W.	6/3-7/10=35 days +16	+ 4
Wm. P. †	6/25-7/10=15 days	

TABLE VII.—SHOWING THE PERCENTAGE OF PROTEIN AND FAT, AND THE NUMBER OF CALORIES IN THE DIETS.

Patient.	P	F	C	P	F	C	P	F	C	P	F	C	P	F	C	P	F	C	P	F	C	P	F	C															
John C.	June 11	1.75	2.00	414	June 13	1.75	2.00	414	June 25	2.85	561	2.14	2.42	417	July 6	2.10	2.40	518	July 10	3.00	571	2.08	2.82	560	July 13	2.57	2.97	579	2.31	2.62	556	August 5*	2.46	2.14	518				
	June 3	1.70	1.90	540	June 13	1.84	0.52	435	June 29	2.16	0.60	437	July 1	2.20	500	July 13	2.10	0.60	515	July 22	2.10	0.60	390	July 26	2.10	0.60	375	July 28	2.10	0.60	445	2.24	0.64	463	August 5	2.24	0.64	470	
Helen B.	June 3	1.50	1.71	450	June 13	1.76	1.50	515	June 25	1.66	1.90	510	June 29	1.91	2.19	593	July 10	2.09	2.38	619	July 22	2.26	2.57	645	July 26*	2.42	2.76	684	July 28*	2.50	2.85	696	2.50	2.85	696	August 6*	2.66	2.28	640
	June 3	1.80	2.10	600	June 11	1.92	2.19	621	June 29	2.03	2.90	800	July 2	2.18	3.10	830	July 20	1.81	2.58	590	July 24	1.86	2.64	708	July 26	2.18	3.10	830	July 29	2.18	3.09	912	2.10	2.70	870	August 6	2.33	2.66	853
Walter McK.	June 23	2.10	2.40	860	July 5	2.10	2.40	860	July 10	2.10	1.20	710	July 15	2.10	1.20	590	July 21	2.10	1.80	665	July 25*	2.10	1.80	685	July 29*	2.24	0.64	544	August 1*	2.38	0.68	553	2.52	0.72	562	August 7	2.52	0.72	562
	June 13	1.65	0.47	365	June 29	1.81	1.05	426	July 2	2.02	0.57	387	July 6	2.08	1.19	491	July 15	2.04	1.04	516	July 22	2.14	1.09	553	July 26	2.26	1.18	575	August 2	2.37	1.23	665	2.46	1.22	644	August 7	2.46	1.24	595
John P.	June 11	1.83	2.09	700	June 13	2.33	2.66	680	June 23	1.66	1.90	554	July 10	1.83	1.57	525	July 15	1.83	2.09	580	July 24	2.10	2.35	619	July 29	2.33	2.00	588	August 2	2.42	2.07	599	2.42	2.76	671	August 5	2.52	2.16	728
	June 11	1.83	2.09	700	June 20	2.33	2.66	680	June 23	1.79	2.04	573	June 25	2.16	2.47	632	June 29*	1.75	2.00	588	July 10	1.75	2.00	569	July 22	1.75	1.50	515	July 28	1.92	1.64	536	2.00	1.71	546	August 5	2.33	1.33	518
John W.	June 3	1.83	2.09	560	June 13	2.50	1.60	578	June 23	1.50	1.28	483	July 15	1.66	1.42	504	July 17	1.75	1.50	515	July 20	1.83	1.57	525	July 24	2.00	1.70	546	July 28	2.10	1.75	565	2.00	2.28	606	August 5	2.20	2.30	635
	June 21	2.10	2.40	860	July 5	2.90	3.02	826	July 10	2.38	2.72	792	July 15	2.38	3.40	877	July 21	2.50	2.85	684	July 26	2.66	0.76	470	July 30	2.66	0.76	312	August 1	2.83	0.80	481	August 5	2.80	0.80	570			

P = Protein in diet, per cent.
 F = Fat in diet, per cent.
 C = Calories.
 * = Malt soup used as diluent instead of barley gruel.

Diets usually consisted of milk, dextrinized barley gruel and one grain of sodium citrate to the ounce. Changes in the diet were made on the days indicated, as it appeared necessary.

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REVIEWS.

HYGIENE AND SANITATION. BY SENECA EGBERT, A.M., M.D., Professor of Hygiene, University of Pennsylvania; formerly Professor of Hygiene and Dean of the Medico-Chirurgical College. Seventh edition. Pp. 554; 160 engravings and 5 plates. Philadelphia and New York: Lea & Febiger, 1919.

THE war if it has done nothing else has brought home the importance of hygiene and sanitation. As armies fail if they do not maintain a high standard of sanitation and hygiene, just so do civilian communities suffer if they do not enforce strict sanitary laws.

The seventh edition of this well-known work comes at a very opportune moment, and must appeal especially to ex-service men. To the present work have been added about nineteen engravings and about twenty-nine pages. The table of contents remains unchanged, and includes as headings, air, water, food, stimulants and beverages, personal hygiene, school hygiene, disinfection, quarantine, sewage, industrial hygiene, vital statistics and the examination of air, water and food. The text of the first two hundred and fifty pages remains practically unchanged. Several new paragraphs are introduced, dealing with the question of vitamins. The author in his preface makes a plea for his plan of retaining much of the old material and having omitted some new matters. This is to be regretted, for much that is new and sound by experience and experiment might have been included. The biggest change is made in the chapter on military hygiene, in which some statistical facts and other matter have been added to the text as it formerly read in the sixth edition. Some new engravings have been inserted in this chapter. The paragraphs on sewage disposal have received some revision, and are worth while.

The book remains a well-done manual, covering the field of sanitation and hygiene. The subject-matter is dealt with in a consistently sound fashion, along well-recognized lines, and holds the reader's interest, although handling material of a stabilized character. Seven editions is no mean record for a work on hygiene and sanitation, a tribute to the character of the book. T. G. S.

MANUAL OF OBSTETRICS. By EDWARD P. DAVIS, A.M., M.D., F.A.C.S., Professor of Obstetrics in the Jefferson Medical College. Second edition. Pp. 478; 163 illustrations. Philadelphia and London: W. B. Saunders Company, 1919.

THERE is undoubtedly a definite place in the medical library for the books known as manuals which are usually of such a nature as to place them between quiz compends and complete text-books. The scope of the volume under consideration is such that the book may be said to be a text-book of obstetrics compressed into a manual. Although it is of a very convenient size it is remarkable how much of real value has been embraced by the author. Of the new material that has been introduced into this edition, anesthesia in labor and the Porro operation are the most practical articles and are well handled. It seems a bit humorous, however, to note that one of the points mentioned in the differential diagnosis of *early* pregnancy is that the fetal movements may be felt and the heart sounds heard *after the sixth month*. The treatment of the early toxemia by means of corpus luteum injections is not mentioned although such procedures as amputation of both breasts and renal decapsulation in the treatment of eclampsia are dignified by their inclusion. The book should continue to be a valuable aid to students who want facts and want them quickly. F. B. B.

ANALES DE LA ACADEMIA DE CIENCIAS MEDICAS FISICAS Y
NATURALES DE LA HABANA, Tom. IV, 1918-1919.

"The Schistosomum Mansoni in Venezuela," Dr. John Guiteras, page 22. Dr. Guiteras calls attention to the recent work of Dr. Juan Iturbe, of Caracas, who discovered the intermediate host of Schistosomum mansoni, planorbis Guadelupensis, and points out the danger of the immigration into Cuba of Chinese, Japanese, Jamaicans and Haitians, among whom the infection is common.

Dr. Agramontes, in the discussion of Dr. Guiteras's communication, calls attention to the discovery of Clonorchis sinensis for the first time in Cuba by Dr. P. L. Querens.

The "Influence of Animal Experimentation in the Progress of Medical Science," Dr. Aristides Agramontes, page 35. Dr. Agramontes, in a carefully prepared communication on the subject, after giving a brief historical sketch of the important discoveries made in medicine and physiology, based on animal experimentation, also emphasizes the erroneous attitude taken by antivivisectionists on this point.

"The Microorganisms of Influenza," Dr. Leonel Plasencia, page 473. Dr. Plasencia claims to have discovered a new microorganism, Bacillus influenza motili, as the cause of influenza.

Dr. M. Martinez Dominguez, in a communication to the Academy, "Upon the Bacteriology of Grippe," page 560, shows by cultural characteristics and experiments on man that the bacillus of Dr. Plasencia is a microorganism related to *Bacillus cloacæ* and that it has no etiological significance to influenza.

Dr. Manuel Ruiz Casabo, in another communication to the Academy, "Notes upon the Present Epidemic of Influenza," page 449, regards the present epidemic of influenza as the classic influenza, or grippe, and that bacteriological investigations commonly show the presence of the *Bacillus influenza* of Pfeiffer in association with pneumococcus, staphylococcus and micrococcus catarrhalis.

"Etiology and Treatment of Strabismus," Dr. Francisco Fernandez, page 56. According to Dr. Fernandez, concomitant strabismus is the result of a defect in the proper fusion of the images in the brain. Muscular insufficiency, myopia, hypermetropia and other affections of the eye are only predisposing factors to strabismus.

"Concerning the Center for Hunger and Thirst," Dr. Jorge Le Roy, Dr. Jose Valdez Anciano and Dr. Felipe Garcia Cañizares, page 898. According to these authors, though the plexus of Auerbach is of importance, the center for hunger and thirst is in the medulla, the pneumogastric and splanchnic nerves acting as regulators.

D. R.

SYMPTOMS OF VISCERAL DISEASE. A STUDY OF THE VEGETATIVE NERVOUS SYSTEM IN ITS RELATIONSHIP TO CLINICAL MEDICINE. By FRANCIS MARION POTTENGER, A.M., M.D., LL.D., F.A.C.P., Medical Director, Pottenger Sanatorium for Diseases of the Lungs and Throat, Monrovia, Calif.; Professor of Diseases of the Chest, College of Physicians and Surgeons, Medical Department, University of Southern California, Los Angeles, Calif. Pp. 317; 86 illustrations and 9 plates. St. Louis: C. V. Mosby Company.

It is decidedly refreshing to pick up a book which is distinctly different from the average medical text-book, a book which deals with a phase of medicine which is considered but too briefly, if at all, in our present-day didactic text-books. In this book by Dr. Pottenger a new field has been opened up to those who have not followed carefully the work of Mackenzie, Head and several others. It is written by a man who, although a specialist in pulmonary diseases, has studied internal medicine not only from the one side of pulmonary diseases but from the many sides of diseases of all the organs. He well shows that it is impossible to have as a specialty the study of one organ, and, as he says, "the human body is a unit and one part cannot be diseased without affecting other parts. No organ can be understood except in its relationship to other organs in the body as a whole."

The book is arranged in three parts: Parts I and II are the clinical study of the relation of the vegetative nervous system to diseases and symptoms and a study of the viscerogenic reflexes, while Part III is a very technical discussion of the vegetative nervous system. The most obvious criticism of the presentation of the subject which comes to the mind of the reviewer is that there is more or less repetition of many of the statements of facts and theories in the various parts of the book. In a monograph of this size repetition must be expected, but it does seem as though the same things are dwelt upon a bit too repeatedly.

The chief defect of the work itself is that many of these reflexes, such as the viscerosensory, visceromotor and so on, are only demonstrable in cases with well-marked disturbance of the vegetative nervous system. Certainly, the ordinary physician without the very keen power of observation and well-developed clinical sense of Dr. Pottenger will be unable to demonstrate some of these reflexes which he gives you the impression are relatively simple and extremely easy to demonstrate.

J. H. M., JR.

THE PREVENTION OF DENTAL CARIES AND ORAL SEPSIS. By H. P. PICKERILL, M.D., Ch.B., M.D.S. (Birm.), L.D.S. (Eng.), Professor of Dentistry and Director of the Dental School in the University of Otago. Second edition. Pp. 374; 74 illustrations and 12 tables. New York: Paul B. Hoeber, 1919.

THIS is the second edition of the Royal College of Surgeons' Cartwright Prize Essay for 1910, and represents fifteen years' research into the etiology and pathology of dental caries. The writer, being a New Zealander, has been afforded exceptional opportunities for comparative studies of this disease in civilized and relatively uncivilized races. Among the Maori race, living under natural conditions, the number of persons affected with dental caries is comparatively small, while in civilized, modern races the percentage is as high as 98. Also the number of teeth affected with caries in each individual is far less in those leading natural lives than in those leading artificial or highly civilized lives.

The great part of the book is a description of exhaustive studies upon the bacteria of the mouth, the structure of the enamel of the teeth and the physical and chemical properties of the saliva. Pickerill's conclusions from his researches may be summed up as follows:

1. The two essential, attacking forces in dental caries are (a) the acid-forming organisms of the mouth and (b) the presence of fermentable carbohydrates.

2. Individual susceptibility to dental caries depends, to a great extent, upon differences in the structure, hardness, density, permeability and solubility of the enamel.

3. Studies of the saliva show that practically all the normal constituents of the saliva are, if present in sufficient amount, of value in protecting the teeth against the occurrence of dental caries; that acids, and particularly the natural organic acids, are the stimulants which excite the greatest amount of these protective substances per minute, and, moreover, give rise immediately and for a considerable time afterward to an increased alkalinity of the mouth.

4. The carbohydrates of the food being the source of the acids which initiate dental caries, the question of the lodgeability of carbohydrate foods upon the tooth surfaces is important. The lodgeability of carbohydrates upon the teeth does not depend upon the amount of inert or fibrous matter they contain, but their lodgeability or harmfulness is in direct relation to their alkalinity. In other words the saliva will more readily wash away carbohydrate foods having an acid reaction than those having a neutral or alkaline reaction.

As measures for the prevention of dental caries in civilized races the author has the following suggestions:

In order to prevent the retention of fermentable carbohydrates on or between the teeth, and so eliminate or very considerably reduce the carbohydrate factor in the production of caries, starches and sugars should never be eaten alone but should in all cases either be combined with a substance having a distinctly acid taste or they should be followed by such substances as have an "alkaline potential," and the best of these are undoubtedly the natural organic acids found in fruits and vegetables.

Both educational and legislative measures are also advocated. The educational measures suggested comprise definite lessons in oral hygiene by the teachers in primary schools, education of medical men as to its importance, and, finally, more thorough education of the dental student in the technical side of the subject. The author suggests the taxation as luxuries of sweetmeats, confectionery and fine white flour in order to decrease their general use, and legislation fostering the culture, carriage, freight and importation of fruit and fresh vegetables, so that such articles, especially fruit, may come to be regarded as common, ordinary and necessary constituents of every meal instead of being, as at present, regarded as unnecessary and too expensive for common and constant use. In addition, the prevention of dental caries must be made one of the important branches of the public health service.

Many of the problems of dental caries are to be regarded as having been by no means solved by the researches of Dr. Pickerill, and other workers in this field will no doubt disagree with many of his conclusions. At the same time his book must be looked upon as a valuable contribution to this intricate subject.

R. H. I.

A MANUAL OF OBSTETRICS. By JOHN COOKE HIRST, M.D., Associate in Obstetrics, University of Pennsylvania. Pp. 485: 216 illustrations. Philadelphia and London: W. B. Saunders & Co., 1919.

THIS manual, which is offered primarily for the use of students, carries one over the whole range of obstetrics in a lively manner. While a certain amount of condensation of material has been necessary, the chapters so limited will still be found to contain a sufficient amount of information to one who wishes to review the subject rapidly. For the treatment of obstetric emergencies, concise directions are given as to the method of treatment which has proved most satisfactory in the hands of the author. Abnormal pelves have been divided into five groups, based upon the predominating deformities; this classification is considered as easy for the student to remember and sufficiently accurate for all practical purposes. The chapter on the mechanism of labor should make this usually mysterious process easily understood by the average student. The illustrations, chosen from many sources, have been well selected to supplement the text. The description of a method for chemical analysis of the blood on pages 192 et seq. could well have been omitted from a book of this type. The word inlet is evidently mistakenly used for the word outlet, page 223.

While it seems at times as though there were sufficient textbooks on obstetrics available, yet such a manual based on many years' experience in didactic and clinical obstetrics will take a well merited place in the obstetrical library. P. F. W.

ACCOMMODATION AND REFRACTION OF THE EYE. By EARNEST CLARKE, M.D., Ophthalmic Surgeon to the King George Hospital, London. Fourth edition. Pp. 250; 92 illustrations. New York: William Wood & Co., 1918.

THIS work purports to be an elaboration of the lectures on refraction and accommodation as given by Mr. Earnest Clarke at the Central London Ophthalmic Hospital and Medical Graduates' College.

As a work to be studied by one with some familiarity in the subjects dealt with, this book can be highly recommended. We doubt, however, the advisability of the tyro endeavoring to master these subjects from this volume.

The author, in his endeavor to keep the volume within a small compass, has sacrificed in parts clarity for the sake of brevity. As a rule, the outlines suggested by him for the treatment of the various forms of refractive error are wholesome, and if exception is to be taken at all, it is that he too liberally reduces the hypermetropic correction. B. F. B.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Achylia Gastrica.—FRICKER (*Corr. Blat. f. Schweiz. Aerzte*, 1919, xlix, 1657). Achylia is rare in early life but common after middle life, and often displays no symptoms for a long period. Gastrogenous diarrhea is one of the most common symptoms. The diagnosis is easily made by a test-meal. Occult blood is rarely found. Exploratory laparotomy seemed advisable in two cases and pieces of stomach wall were obtained for histological study. In each instance marked changes were present in the mucosa, especially in the secreting cells. The cause of achlorhydria and achylia is thought by the author to be a gastritis atrophicans not only in simple achylia gastrica but also in instances of carcinoma and pyloric stenosis associated with achylia gastrica.

Suppuration and Gangrene of the Lung.—WESSLER (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1918) has analyzed 100 (personally observed) cases of lung suppuration. About 94 per cent. of the cases fall into two groups: (1) those due to the aspiration of septic material into the bronchi during operations or in states of unconsciousness and (2) those dependent on the various primary lung infections. Twenty-one per cent. followed tonsillectomies and 37 per cent. were postpneumonic. Clinically there are usually foul expectoration, persistent fever and leukocytosis, and in bronchiectasis, the early development of clubbed fingers (as early as six weeks). The physical signs are notoriously uncertain. Signs of consolidation and cavitation are important if present. The extent and locality of the process is ascertained readily by roentgenó-

grams. The prognosis depends somewhat on the etiology. Nine post-operative abscesses recovered spontaneously. In each instance either cure was accomplished in two months or the process went on to the chronic stage with the usual sequelæ. Commonly empyema results and occasionally septic brain abscesses occur. The prognosis of postpneumonic instances is bad, the process leading to induration and bronchiectasis. Medical treatment consists of quieting the cough, and drainage of the abscess by change of posture. Surgical treatment may profitably be postponed for several months in instances of acute abscess. Thoracotomy with drainage or lobectomy may be attempted after the disease has become chronic. Five in the series were cured by lobectomy. Very little can be expected of thoracotomy with drainage.

Eosinophilous Myocarditis in Diphtheria.—NUZUM (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1925) by various blood stains found eosinophiles in the myocardiums of seven out of twenty-nine hearts of children dead from diphtheria. None were found in hearts of children dead from other infectious diseases. The eosinophilia had apparently no relation to serum treatment nor to the severity of the clinical symptoms. Eosinophilia was never observed in the structures of the conducting system. The His bundle was studied carefully and no changes characteristic of diphtheria were found, although slight changes and especially swelling may account for the frequent cardiac irregularities in diphtheria. Other factors, as myocardial and cardiac nerve lesions, may play an important part in the causation of arrhythmias. The cause of the eosinophilous myocarditis is not known. The author reviews the various theories, and concludes that it is a result of positive chemotaxis.

Acute Ascending Paralysis Among Troops.—CASAMAJOR (*Arch. Neurol. and Psychiat.*, 1919, ii, 605) under this heading reports several instances of the interesting malady described by Gordon Holmes and Bashford and Wilson as "acute polyn neuritis." Clinically there is fever from 100° to 103° F., lasting two to four days, accompanied by headache and general pains. This disappears and the patients resume their duties. After four days to a month or even six weeks a paralytic stage makes its appearance, as a rule suddenly. The legs are affected first, then the trunk and arms and finally respiratory paralysis occurs in the fatal cases. Occasionally the VII pair may be involved. The period of paralysis is usually complete in a very few days. The paralysis is flaccid, and if any musculature is spared it is in the distal portion of the limb. The sensory changes are usually of the stocking-and-glove distribution. The sphincters are usually intact. The mortality is fairly high. In non-fatal cases the paralysis slowly disappears and after six to eight months the patient has completely recovered. Pathologically there are congestion and hemorrhage in the arachnoid, thickening of the pia, absence of perivascular infiltration, increase of cellular neuroglia in the central gray, around the root fibers and in the posterior ganglions, beginning degeneration of both a secondary and primary character in the anterior horn cell and some tract cells and marked primary and secondary degeneration of the nerve fibers where they lie in the arachnoid, always most marked in the motor fibers. In the succeeding article KENNEDY (pages 621 to 627) describes the same affection under the title of "Infective Neuronitis."

Antipyretics I, II, III.—BARBOUR and DEVENIS (*Arch. Int. Med.*, Chicago, 1919, xxiv, 611). The Benedict respiration chamber was used to study the respiratory exchange of five normal subjects. The dose of acetylsalicylic acid was 1 gm. or 1 gm. 25, and the experiments were carefully controlled. It was found that the CO₂ production and the O₂ consumption were, in the majority of instances, increased, showing therefore an increased total metabolism. The average heat production increase was 6.1 per cent. over normal controls. The respiratory quotient and the pulse-rate were not altered. After the preliminary study of normal subjects the same dose of the drug was exhibited and the same procedure used in the study of five febrile patients. It was determined that acetylsalicylic acid exhibits marked antipyretic action in febrile subjects contrary to its effect on the normal controls. Heat elimination was increased 38.2 per cent. These experiments show that "acetylsalicylic acid, like other antipyretic drugs, exerts its temperature-reducing action essentially by increasing the processes of heat elimination." "This action of acetylsalicylic acid is exhibited in afebrile stages and during convalescence, with resulting subnormal temperatures." Antipyretics therefore "reduce the body temperature in fever cases (including temporarily afebrile and convalescent phases) but not in normal persons."

SURGERY

UNDER THE CHARGE OF

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Treatment of Metastatic Carcinoma of the Spine by Deep Roentgenotherapy.—PFAHLER (*Surg., Gyn. and Obst.*, 1919, xxix, 236) says that the roentgen rays when applied properly and in sufficient quantity upon deep seated cancer tissue may be expected to destroy the cancer cell, and this cancer cell is replaced by healthy scar-tissue, or fibrous tissue. When the disease is located in the soft tissues, it is replaced by fibrous tissue, and when located in bone it heals by bone sclerosis. As a result of this healing process, the patient is given prolongation of life, and is made more comfortable. One cannot expect the patient to make a complete, permanent recovery, for ultimately the disease is apt to show metastases particularly in the areas not treated.

Megaduodenum.—DUBOSE (*Surg., Gynec. and Obst.*, 1919, xxix, 278) says that a search of the literature finds no recorded case of giant duodenum in an infant. The symptoms in his case began when the child was three days old, and the patient was first seen by Dubose when eight weeks old. Gastro-enterostomy with pyloric occlusion is the operation of choice in partial obstruction at the duodenojejunal flexure in infants

for the following reasons: The dilated stomach is drained into the jejunum. Pyloric obstruction diverts bile and pancreatic fluid into the jejunum and prevents regurgitation into the stomach. Bile, pancreatic, and duodenal fluid with the contained hormones, so greatly needed, are more largely conserved than if the pylorus were not occluded. Regurgitation into the stomach and loss of fluids is lessened through cessation of vomiting—more certainly obtained in gastro-enterostomy with pyloric occlusion than in duodenojejunosomy. Pyloric occlusion is essential. Five months have elapsed since this operation was done, and the infant weighed then 12 pounds and 8 ounces.

Futility of Bridging Nerve Defects by Means of Nerve Flaps.—STOOKEY (*Surg., Gynec. and Obst.*, 1919, xxix, 287) presents a very thorough study of clinical, experimental and anatomical data from the literature and says that the repair of nerve defects by means of nerve flaps has not been definitely supported clinically, as evidenced by a critical study of the reported cases. Experimentally it has been shown that nerve flaps do not serve as conducting paths for the downgrowing neuraxes. Nerve flaps whether central or peripheral are merely degenerated partial nerve segments. Continuity and union of neuraxes does not take place at point of suture. To avoid fallacious deductions it is important to distinguish between the level of the injury to the nerve trunk and the level at which muscular branches arise. Abnormal communicating branches are not rare, particularly between the median and ulnar. Such anomalies must be taken into consideration of any careful study of nerve injuries. Judging from the level of the lesion, muscles may not be presumed paralyzed but should be demonstrated paralyzed. Total movements may not be offered as evidence of return of function. The action of individual muscles must be given. Reports of peripheral nerve injuries, to be of value, must be accompanied by motor, sensory and electrical findings. By the formation of nerve flaps from the central stump a portion of the nerve from which neuraxes must grow is removed. Distal as well as central flaps may sever muscular branches. By reversing the flaps they are taken out of their field. Thus the downgrowing neuraxes are prevented from reaching their muscles through these muscular branches, even were regeneration to take place. The nerve flap method to bridge nerve defects should be discarded in peripheral nerve surgery.

Early Surgical and Orthopedic Treatment of Hemiplegia.—BYRNE, TAYLOR and BOORSTEIN (*Surg., Gynec. and Obst.*, 1919, xxix, 398) says that early operation within two to four weeks, or even after a much longer period, may be indicated in hemiplegia: (a) Where the intracranial pressure threatens medullary strangulation, no matter what the site or nature of the lesion; (b) in extradural hemorrhage, with or without intradural hemorrhage, or cerebral contusion, where cerebral compression threatens life or permanent disability; (c) in intradural hemorrhage of traumatic or spontaneous origin where cerebral compression threatens life or permanent disability; (d) in intracerebral hemorrhage where focal compression threatens life or permanent disability. A subtemporal decompression and evacuation of the clot is a simple procedure and should be used in every case of fresh hemiplegia where the above-mentioned indications are present. If the patient be

unconscious, an anesthetic need not be used, as the shock of the operation is small. Even in old cases of hemiplegia decompression is of benefit. Decompression should be used even in cases due to embolism or thrombosis. The deformities and contractures of hemiplegia can be prevented. Patients with hemiplegia should be put in the same category as anterior poliomyelitis and receive proper orthopedic treatments from the beginning. Plaster splints should be applied immediately to prevent contractures. Massage and exercises are indicated and should be used intelligently. Proper use of the limbs should be shown to the patients and encouraged. In old and neglected cases deformities should be corrected and recurrences prevented.

Gunshot Injuries of the Knee-joint in a Base Hospital.—DAVID (*Ann. Surg.*, 1919, lxx, 290) says that of the gunshot wounds of the knee coming to a base hospital after operation, 56 per cent. remained uninfected and 44 per cent. infected. Of the infected cases, 5 required amputations, with one ensuing fatality. Infection of the joint plays the most important role in decreasing the function of the joint. Early operation at the front, thorough débridement of the wound, removal of foreign bodies and loose bone fragments from the joint, and closure of the capsule of the joint are the most important elements in preventing infection of the joint. Almost 50 per cent. of joints having fractures of the articular surfaces became infected after operation, whereas only 33 per cent. of other types of injury to the joint became infected. Of the high explosive fractures of the condyles of the femur nearly 60 per cent. were uninfected after operation. Fractures of the tibia did not do so well. Joints remaining uninfected after operation for fracture of the articular surfaces had normal motion, to 90 per cent. active motion in 70 per cent. of the cases. Whenever possible, injured or infected joints were actively mobilized after operation, but active mobilization is not practicable in all war injuries of joints. Of the infected joints, all that were by necessity immobilized had only ten degrees or less active motion two months after injury. Of those actively mobilized immediately after drainage of the joint, two had normal motion and the remainder better than twenty degrees of active motion two months after injury.

Surgical Treatment and Prognosis of Empyema Following La Grippe.—LEYVA and LEGENDRE (*Surg., Gynec. and Obst.*, 1919, xxix, 17) say that during the past year they had the privilege of treating in their war service 27 patients suffering from empyema, the empyema in all but one case following la grippe. Eight died and nineteen were cured or are recovering. They studied the cause of the high mortality and concluded that the prognosis in empyema is not based on the nature of the micro-organism causing the condition but principally upon the condition of the lungs. As pleurisy starts early with grippe, they believe it is best for the patients, to treat them medically by aspiration and injection with specific sera, until the pulmonary symptoms have subsided. At this time surgical intervention has every chance of success. The micro-organism causing the pleurisy has no bearing on the type of operation to be performed. In pleurisy developing late in la grippe the pleurotomy opening must be large, extending backward; resection of a rib is a necessity. The classic treatment consisting in drainage without irrigation is the method of choice.

THERAPEUTICS

UNDER THE CHARGE OF

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Meningococcus Meningitis at Camp Lee.—HADEN (*Arch. Int. Med.*, 1919, xxiv, 514) reports a study of 31 cases of meningococcus meningitis occurring at Camp Lee. Twenty-one, or 67.7 per cent., showed unmistakable evidence of a generalized infection before there was a localization in the meninges. The mortality of the entire series was 22.6 per cent. During the period of intraspinal treatment alone and combined intraspinal and subcutaneous treatment the mortality was 37.5 per cent. On the other hand, during the period in which intraspinal and intravenous therapy was employed the mortality was 6.6 per cent. The author believes that meningococcus meningitis, in probably every case, is primarily a generalized infection, with subsequent meningeal localization. The use of immune serum intravenously makes a great advance in the treatment of the disease. He is also of the opinion that prolonged intraspinal treatment is very liable to result in permanent ill-effects from the involvement of the cauda equina and nerve roots. One advantage of intravenous treatment is that it decreases the number of intraspinal treatments necessary, thus minimizing the harmful effects of intraspinal treatment. Haden reports one case in which an active meningeal infection recovered under intravenous therapy alone.

The Activity of American Digitalis.—PRATT and MORRISON (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1606) have tested 28 samples of American grown digitalis and found that the best American digitalis, both wild and cultivated, is equal in activity to the best European. Specimens of high potency have been obtained from Virginia, Nebraska, Wisconsin, Minnesota, Oregon and Washington. The majority of samples of American digitalis examined were of low potency. No less than seventeen out of twenty-five samples of American digitalis were below the standard of strength established by the Pharmacopœia. This is also true of most of the digitalis imported from England and Germany. The average strength of the American digitalis, however, was greater than that of the imported digitalis that they examined. All digitalis should be tested biologically before it is gathered in large quantities for therapeutic use.

The Treatment of Thyrotoxicosis by Means of the Roentgen Ray.—HOLMES and MERRILL (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1693) state that during the past five years they have treated at the Massachusetts

General Hospital 262 patients suffering from thyrotoxicosis by means of the roentgen ray. They think that the results have been sufficiently encouraging to warrant a more general use of this remedy. Of the 262 cases there were 133 patients who, because of insufficient data, were excluded from the analysis of their results. Of the remainder, 34 patients became clinically cured apparently as a result of the treatment. Sixty-eight patients were improved. This group was under treatment for a shorter period of time on the average and received a fewer number of treatments. Fourteen patients were either unimproved or made worse. Of this group, 2 died during the period of treatment from intercurrent disease; 1 died following operation. In one patient myxedema developed, probably as a result of overtreatment. The details of the technic of administration are given in the article. The authors believe that this method of treatment is not without danger. Too intensive treatment, especially in cases in which surgical treatment has been employed, may produce hypothyroidism, with the consequent symptoms of myxedema. Atrophy of the skin and telangiectasis may result in the region treated. The toxemia may be increased to a dangerous degree by the first treatment. Very careful dosage is essential to avoid this. In their summary the authors state that: (1) It is possible to decrease the activity of the thyroid gland and probably to destroy its glandular structure by exposure to the roentgen ray. (2) Roentgen-ray treatment when applied in cases of thyrotoxicosis produces a relief of symptoms and shortens the course of the disease. (3) A study of the basal metabolism before, during, and after treatment is of the greatest importance both as a means of diagnosis and as a check on the amount of treatment to be given. (4) The roentgen ray, accompanied by rest, should be tried in all cases of thyrotoxicosis and should be continued for a sufficient length of time to destroy at least the thymus before resorting to surgery.

Stone in the Kidney and Ureter from the Standpoint of the Clinical Surgeon.—OCHSNER (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1105) advises in his article the administration of distilled water in large quantities in order to prevent the recurrence of kidney stone and renal colic. He states that he has made use of this method in an enormous number of cases, always with the result that the patients escape recurrences. For patients suffering from acute renal colic the use of morphin and atropin hypodermically, followed by the ingestion of two-ounce doses of glycerin with large quantities of distilled water, has seemed to the author to be of value in aiding the discharge of the stones spontaneously, especially when the patient was immersed in a very hot bath.

Results in the Modern Treatment of Diabetes.—GEYELIN (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1202) states that as the result of his experience in the past four years in dealing with many diabetic patients treated according to the general principle laid down by Allen there are certain definite conclusions that can be drawn: (1) Diabetes in its severe and acute form is not limited to the first three decades of life but may be found at any age, although rare in persons over thirty. In his experience it is more common between fifty and seventy than between thirty and fifty. (2) Absolute adherence to the diet is essential

to a maximum degree of successful results in treatment. Otherwise unless the diabetes is very mild there is no hope. (3) Fast days and half-days are of great help in the treatment of the majority of patients, but are not necessary as routine measures in all cases at all times. (4) It is wise for a patient under treatment to realize that he is not a normal person on a normal diet and to regulate his mental and physical activities (and therefore his caloric output) by his caloric intake. (5) Exercise should be advised only in exceptional cases and in proportion to the amount of energy afforded by the caloric intake. Rest rather than exercise should be urged. (6) Long-continued diets overbalanced in fat (180 gm. and over) are harmful and their harmful effect is insidious. Aside from their immediate effects in the production of acidosis and glycosuria they have a depressing effect on tolerance. This effect is overcome only by long periods of low caloric intake. (7) We have no cure for diabetes, but we have a greatly improved method of treatment, particularly as regards prolongation of life and the avoidance of surgical complications, as many observers who have employed the general principles of treatment advanced by Allen will testify.

PEDIATRICS

UNDER THE CHARGE OF

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The Child and the State.—SHAW (*Arch. Ped.*, August, 1919) says that a child should have the right to intelligent consideration before he is born, to be born well and to be kept well. To insure this is the purpose of all child welfare work. The State should give to all children a sound and liberal education. Every child should come periodically under direct medical and dental supervision, and if found defective should be followed up. Every child found malnourished should somehow or other be nourished and every child found verminous should somehow or other be cleansed. Skilled medical treatment should be available for every sick, diseased or defective child. Every child should be educated in a well-ventilated classroom, or in some form of open-air schoolroom or classroom. Every child should have daily, organized, physical exercise of appropriate character. No child of school age should be employed for profit except under approved conditions. The school environment and the means of education should be such as can in no way exert unfavorable or injurious influences upon the health, growth, and development of the child. Dr. S. Josephine Baker has outlined a broad scheme of reconstruction and the child. She would have in each State a department of child welfare of equal importance with other State departments. The department should be divided into the following bureaus: (1) A bureau of child-caring institutions, which would supervise orphan asylums, day nurseries, boarded-out babies,

and widows' pensions; (2) a bureau of mental hygiene, which would have charge of all matters pertaining to mentally defective children; (3) a bureau of delinquency where the relation of crime to health would be studied and the prevention of crime in children would be supervised and the courts for children would be supervised as well; (4) a bureau of recreation, which would supervise playgrounds, physical training and play; (5) a bureau of child labor with the supervision of the child in industries and the carrying out of the child labor laws from the point of view of the child and not of the employer; (6) a bureau of child hygiene with the responsibility of the health of the children and their care from the prenatal period to adolescence. This bureau would control midwives, prenatal care, prevention of infant mortality, child welfare stations, health supervision of the child of the pre-school age, medical inspection and examination of school children; (7) a bureau of child legislation to prepare a children's code which would consist of all essential legislation to protect the child from the prenatal period to adolescence.

Stammering.—KENYON (*Am. Jour. Dis. Children*, December, 1919) contends that stammering in most cases begins in early childhood as a perversion of the normal processes of speech development. This perversion of the normal speech processes is dependent on emotional disturbances arising from the necessity of developing the speech function under the trying conditions of social interrelations. Thus there are aroused in the child more or less profound manifestations of so-called social emotions. Behind this exciting cause often lie congenital foundations and environmental conditions, which tend to encourage the natural childish tendencies to excitability and emotionalism. Natural childish characteristics—impulsiveness, lack of self-control, relative absence of knowledge and reasoning, apprehensiveness—as well as the doubtful, wavering, clumsy, state of partial development of the speech function, both constitute factors which help to render the child susceptible to this manner of speech perversion. The immediate psychology of the incitation to stammering involves emotional excitement, mental confusion, and the impulsive effort to talk while in this uncertain state of mind. The result is a speech panic, in which normal control of the peripheral speech machine is for the moment lost. In the background of this immediate mental picture lie various disturbing phenomena which add to the mental confusion. The beginning perversions of the speech act are often repeated; the stress of mind behind them becomes a more or less constant status of mind. These mental and physical perversions play a harmful part in the general mental and physical physiological processes of development. Thus the susceptibility to emotionalism and excitability slowly increase both as to uncontrollableness and to intensity, as well as to the physical manifestations in the peripheral organs of speech. All of this cannot go on for months and years without having its influence in perverting the development of the character in general. The advanced stammerer becomes a stammering person, rather than an entirely normal person who stammers. This fact renders the complete eradication of the disorder exceedingly difficult and calls for the beginning of treatment at the earliest possible time, preferably at the beginning of the manifestations.

Carotinemia.—HESS and MYERS (*Jour. Am. Med. Assn.*, December 6, 1919) report two cases in which this condition was found. Their attention was attracted by the yellowish complexion, which was not confined to the face but involved the entire body, with the most marked coloration of the hands, which also showed distinct signs of desquamation. The sclerotics were not at all involved. The urine was amber and the stools normally yellow. These cases appeared in a ward of about twenty-five infants and it was noted that these two babies were the only ones receiving a daily ration of carrots in addition to their milk and cereal. Then carrots were added to the dietary of two other children of about the same age. One, after an interval of about five weeks developed a yellowish tinge to the skin and after two more weeks the second infant developed a similar tinge. On omission of the carrots the skin gradually lost its yellow color and in the course of some weeks regained its normal tint. The blood as well as the plasma were found to be distinctly yellow. The pigment was soluble in purified petroleum benzin. It was evident that there was present in these cases a systemic pigmentation brought about by the introduction of an excessive amount of carotin into the body. The pigment is non-toxic and leads to no physiological disturbance. Not only carrots but also any food which contains carotin in high degree may bring about this condition. The urine becomes a yellower tint.

Antineuritic Vitamin.—DANIELS, BYFIELD and LOUGHLIN (*Am. Jour. Dis. Children*, December, 1919) publish the results of their observation on the babies in their clinic. They found that the addition of the antineuritic vitamin obtained from wheat embryo to the diet of babies supplied with food furnishing an adequate number of calories stimulated growth. The beneficial influence of adding a specially prepared vegetable soup in sufficient quantity as part diluent in the milk, modification for infants is apparently due to the presence of the antineuritic vitamin contained therein. Both the alcoholic soluble material of the dried soup vegetable, and the water extract stimulated growth. The fact that the artificially-fed infant requires a larger amount of food than the breast-fed infant appears to be due to the relative paucity of diluted cow's milk in the antineuritic vitamin. It is probable that failure to gain in infants and young children is often the result of an insufficient amount of the antineuritic vitamin in the food. The diets of the young should be more carefully scrutinized with this in mind.

Chemical Examination of the Blood in Children.—CHAPIN and MYERS (*Am. Jour. Dis. Children*, December, 1919) publish their observations on the chemical examination of the blood of one hundred and forty-nine children. Thirty-eight of these were nephritics and six were diabetics. The results were practically the same as those that have been obtained in the adult, although the kidney of the child would appear to act somewhat more efficiently than the kidneys of the adult, resulting in slightly lower normal figures for the sugar, urea, creatinin and uric acid, and a slightly better phenolsulphonephthalein test. Along this line it is shown that nephritis in children does not result so quickly in urea retention as in the adult and the prognosis is therefore more favorable in early life than in later life. Also creatinin retention rarely occurs in

children, being found in only four cases of this series. Of these two died of symptoms typical of interstitial nephritis. The authors regard the blood urea as a very helpful prognostic test in the nephritis of childhood. The results of the phenolsulphonaphthalein test are usually in accord with the clinical findings and the blood urea. The carbon dioxid combining power of the blood is a very reliable method of ascertaining the severity of the acidosis in the diarrheal acidosis.

OBSTETRICS

UNDER THE CHARGE OF

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Frequency of Shoulder Presentation in Different Countries.—IPPOLITO (*Gazetta degli Ospedali e dalle Cliniche*, Milan, March 2, 1919) has collected statistics from six different countries showing that the proportion of shoulder presentation ranges from 0.35 per cent. in America, 0.36 in England, 0.58 per cent. in Germany, 0.66 in France, 0.71 in Austria. On the other hand Italy has an average of 1.40 per cent. shoulder presentations. In twenty years' practice in Sicily in 10,000 deliveries Ippolito encountered shoulder presentation in 0.2 per cent. Comparing the various races it is observed that shoulder presentation becomes less frequent the taller the mothers. While least common among Anglo-Saxons, it occurs most frequent among the Slavic races of Austria. However, the distance between the lower margin of the xiphoid appendage and the upper margin of the symphysis pubis is remarkably constant in women, irrespective of their height. Sicilian women are short but the shortness is in the legs, the length of the trunk and the distance between the xiphoid cartilage and the pubes are rather above than below the average. The writer insists then that the xiphopubic measurement is a very important measurement in obstetric practice. He believes that women are useful in preventing abuses among the poor working women in factories, improperly clad and wearing corsets.

The Transmission of Rabies to the Fetus.—REMLINGER (*Bull. de la Acad. de m d.*, April 8, 1919) has made experiments which confirm Konradi's results. When rabies is inoculated into animals they may not appear out of health for from one to three months, but the young born during this time show rabies and may have died before the mother contracts the disease. In Remlinger's experience one animal developed rabies one hundred and twenty-two days after the inoculation. This was sixty-eight days after the birth of the young and thirty-eight days after the death of the last one of the young. In some cases a year elapsed before the mother died from rabies contracted from the fetus. Young animals may be apparently healthy and yet if infected in the uterus may develop rabies at any time without further contact. It has

often been said that an animal that has never been exposed to the bite cannot acquire rabies but the experiences related illustrate the fact that the fetus might become immunized by small quantities of the rabies traversing the placenta. In some cases it is thought that rabies produces other clinical pictures than that of typical hydrophobia or paralytic rabies.

The Corpus Luteum in Neurologic Practice.—CLIMACO (*Endocrinology*, March, 1919) employed corpus luteum in some cases of male neurasthenics. Organic nervous diseases and the early stages of dementia precox were treated. In these no result was obtained. It had no effect upon the blood-pressure where arteriosclerosis was present. The best results were obtained in young females, less successful in the natural menopause and where a surgical menopause had been brought about there were no results. The drug did better when given by mouth. Two grains was as large a dose as indicated. The best results were seen in cases where there was evidence that the native corpus luteum was still present, but the giving of this cannot replace the natural functions. If menstruation is discontinued because the secretion of a gland, such as the pituitary, is disturbed corpus luteum will not bring on menstruation. The writer believes that this substance has a specific action and that administered extracts do not have the same success as the native hormone, but that the extract stimulates the native corpus luteum to function.

Hemorrhage of the Newborn Successfully Treated by Transfusion.—LOWENBURG (*Jour. Am. Med. Assn.*, May 31, 1919) reports the case of a girl, two days old, brought to the hospital bleeding profusely from the mouth, nose and rectum. The attending physician reported that the child had hematemesis the second day after birth. The child when admitted was very weak and pale and the cause of the bleeding could not be found. Ten cubic centimeters of sterile horse serum was immediately administered and under the skin normal salt solution. The child continued to bleed. Examination of the mouth and nose revealed nothing to explain further bleeding. The child was apparently moribund and stuporous, dissolution seemed to be a matter of minutes. Immediate blood transfusion was decided on. The blood was injected directly into the longitudinal sinus at the posterior angle of the anterior fontanelle. The infant was removed to the operating room, the head shaved, iodine applied over the fontanelle, 80 c.c. of whole human blood. During the operation the patient ceased to breathe and was thought to be dead. The heart sounds could still be heard. Eighty cubic centimeters more of blood were injected directly into the skin of the abdomen. Artificial respiration was used and after several gasps the child breathed. The color of the child grew steadily better, the bleeding ceased almost immediately. A second transfusion was contemplated but proved unnecessary. The child went on to recovery, but had for some time an irregular temperature. Examination of blood in the beginning of the child's treatment showed hemoglobin, 20 per cent.; red cells, 1,400,000; white cells, 12,000. On March 19, 1919, hemoglobin, 65 per cent.; red blood cells, 2,360,000; white blood cells, 10,000,000. The differential count was of no interest. On April 1, 1919, hemoglobin, 80; red blood cells, 3,600,000; white blood cells, 8200.

To What Extent Must We Depend upon the Microscopic Examination to Support the Diagnosis of Ectopic Pregnancy.—CATURANI (*Am. Jour. Obst.*, June, 1919) has studied 100 specimens by microscopic examination to determine the presence or absence of ectopic pregnancy. These specimens consisted of Fallopian tubes and ovaries removed after the clinical diagnosis of ectopic gestation had been made. Of these 85 produced positive microscopical evidence of the condition. The ragged appearance of the tubes and their rupture is almost pathognomonic of ectopic pregnancy. In 42 cases of rupture only 1 was negative. Where there has been complete tubal abortion and hematosalpinx which has persisted for some time, it is difficult to find positive evidence of ectopic pregnancy. In any considerable number of cases submitted to careful microscopic examination the percentage of negative cases is small. In hematosalpinx and hemocele arising from causes other than pregnancy microscopic examination is not always conclusive. The old teaching that hematosalpinx and hemocele are nothing but accidents of ectopic pregnancy must be revised. It is safer to take the ground that ectopic pregnancy causes hemocele unless the contrary can be proved, clinical data remain of the greatest importance.

GYNECOLOGY

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Roentgen Therapy in Benign Bleeding.—The results that have been obtained in the gynecological department of the University of Zurich during the years from 1914 to 1918 in the treatment of benign uterine hemorrhage by means of the roentgen ray have been presented by MANDACH (*Corres.-Blatt f. Schw. Aerzte*, 1919, xlix, 1449) with much enthusiasm. During this period there were 45 cases of climacteric bleeding in which there were no demonstrable pathologic changes in the uterus or the type that is usually designated chronic metritis and which were very rebellious to internal medication. The amount of the treatment varied to some extent with the age of the patient although as a whole the average patient required 4 series before results were obtained. The series that was used consisted of a five-minute radiation in each of three fields on one day, followed radiation in three different fields on a following day and finally in three other fields on the third day. Between series there was a three weeks interval. The details of the technic that was followed are fully described by Mandach but need not be considered here. Suffice it to state that of the 45 cases of metro-

pathic bleeding, complete amenorrhea was obtained in 41; in three patients there was amenorrhea for a few months and then the menstruation returned but in very small amount, while in one patient menstruation continued unchanged in spite of the fact that she had been subjected to 16 series. Of course in all of these patients a preliminary curettage was performed in order to rule out the possibility of a malignant tumor being the cause of the disturbance. The results that were obtained in uterine fibroid cases were also very satisfactory. There were 168 cases that were subjected to the rays, most of which were bleeding freely when the treatment was undertaken. Of these patients there are 108 that have not had any bleeding for over a year, 52 have been free from bleeding for over three months but it has not yet been a year since the last treatment, so that it is too early to tell the ultimate result. Eight patients have had a return of the bleeding, but in four of these a single massive treatment served to cause a permanent amenorrhea, while in the remainder the treatment was absolutely without effect. These results are certainly very satisfactory when we consider that these patients have been freed from their chief symptom, bleeding, without any danger to life during the course of their treatment. Many of these patients had only 20 to 30 per cent. of hemoglobin when they began treatment, but the blood constantly improved and by the time the treatment was completed they were in such a condition as to be able to carry on their usual duties. The question is often asked relative to the manner in which the roentgen rays produce these results, that is, whether the influence of the rays is on the uterus itself or whether it is merely by the effect on the ovaries that the amenorrhea is produced. Mandach states that in his work he has paid special attention to the size of the uterus before and after treatment and he concludes that there is practically no change in the uterus, so far as size is concerned, in the large majority of cases. Therefore he believes that the maximum and principal effect of the rays is due to the ovarian atrophy which is analogous to a castration.

Renal Fluoroscopy at the Operating Table.—BRAASCH and CARMAN (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1751) comment upon the difficulties involved in many cases of renal stone of actually finding the calculus after the patient is on the table and the kidney is exposed. It is apparent that a more accurate method of examination of the kidney at the time of operation is desirable since the usual roentgenographic examination at the operating table is an awkward procedure and requires too much time. It would seem that if fluoroscopic examination when the kidney is brought out of the wound could be made practical, the various difficulties surrounding lithotomy would be readily overcome. Taking advantage of the recent improvement in fluoroscopic apparatus, they have employed for this purpose a machine which is essentially the same as that used in the base and field hospitals of the army, with certain minor changes which make it adaptable to civilian practise. Such an instrument consists of a transformer and autotransformer enclosed in a metal cabinet mounted on large castors for portability. To the cabinet is attached a tube stand with a horizontal arm having universal joints for supporting the tube. The tube is of the Coolidge radiator self-rectifying type, mounted in a lead glass shield. The unit is small and

compact, requiring less than $2\frac{1}{2}$ square feet of floor space. It is of light weight, is portable, and has no moving parts which might cause noise and vibration. The current is turned on and off either by a hand or a floor switch. These portable units may be operated from the ordinary lamp socket without special wiring. As an essential preliminary in the technic, the roentgen-ray operator should wear goggles of smoked glass for about fifteen minutes before the observation is to be made in order that he may have the necessary dark-accommodation and retinal perception. The roentgen-ray unit should be placed as close to the operating table as possible and the rays focussed through a small diaphragm so that they will pass through the delivered kidney on the fluoroscopic screen. When the fluoroscopist is ready to make the roentgenoscopic examination, the hooded screen held in the left hand is placed over the eyes and the goggles are removed and the current is turned on by means of a foot switch. In the right hand is held a sterilized metal-tipped rod 18 inches long with which the fluoroscopist accurately points to the stone shadow in the kidney. The exposure is short, requiring little more than a flash and the various details can be arranged so that there is no interference with surgical asepsis.

Etiology of Tubal Pregnancy.—MILLER (*Surg., Gynec. and Obst.*, 1919, xxix, 560) has had a dozen or more cases with a history about as follows: A woman misses her period and not wishing to go through pregnancy, begins after a few days to take drugs to bring on menstruation or to produce an abortion, or perhaps she introduces catheters or other bodies into the uterus. After an interval of a few weeks, she exhibits the signs and symptoms of a tubal pregnancy and operation shows this to be the true condition. The number of such cases which he has had has been so great and the histories so typical that he has been forced to the conclusion that there is a causal relation between the taking of oxytocics, and perhaps the other measures commonly employed in the production of an early abortion, and tubal pregnancy. Although he has no definite or experimental data to confirm such a conclusion, the arguments in its favor can be briefly stated as follows: (1) Impregnation can occur just before a menstrual period. (2) The length of time between the fertilization of the ovum and its implantation in the uterine cavity is generally given as between seven and nine days, but it may be longer. (3) Anything which interferes with the passage of the ovum along the Fallopian tube is recognized as a cause of tubal pregnancy, such as tumors in the uterine wall, chronic salpingitis and torsions of the tube. Ergot and similar drugs produce contractions of the uterine muscle and perhaps of the tube and the introduction of foreign bodies into the uterine cavity likewise produces such contractions. These contractions of the uterus must interfere with the passage of the fertilized ovum down the tube and thus they would tend to the production of a tubal pregnancy. Thus it seems entirely possible to produce a tubal pregnancy in the attempts to bring on an early abortion.

Temporary Sterilization of the Female.—In those cases where it is advisable to produce a temporary sterilization of the female, TURENNE (*Surg., Gynec. and Obst.*, 1919, xxix, 577) of Uruguay has suggested the

following operation: After the integrity of the adnexa is established, the broad ligament is held with two hooked forceps in a way to present amply its anterior surface. Ten or 15 millimeters from the lower tubal border and near the ostium he makes a 15 or 20 millimeter incision in the anterior layer of the broad ligament, separates the edges of the incision and hollows out in the cellular space which separates the two layers of the ligament a little pocket sufficient to contain the tubal ostium. The ostium is folded in this pocket and sutured and for greater security it is fixed to the ligament at a separate point near the tube. In this manner the organ retains sufficient mobility, it is not violently kinked and prolonged observation does not show any circulatory disturbance of any sort. With this technic, one can be certain of being able later to do with ease a salpingostomy and to adjust the opening to the ovary.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Fate of Bacteria Introduced into the Upper Air Passages.—A study of the localization, growth and disposal of microorganisms in the upper respiratory tract may aid materially in the study of the carrier problem, chiefly by indicating that for the development of a carrier state some anatomical anomaly or pathological condition of the upper air passages is a primary requisite. This work which was carried out with cultures of *sarcina lutea*, may not be directly applicable to virulent organisms. BLOOMFIELD (*Am. Rev. Tbc.*, 1919, iii, 553) employed a culture of *sarcina* which grew well in symbiosis with the common mouth organisms. The individuals used in the work had only minor abnormalities of the upper air passages, and none showed *sarcina* in preliminary cultures from the regions studied. He found that *sarcina* swabbed on the tongue practically disappeared within one hour. In the nose, a heavy inoculation persisted longer, but in only one out of five instances, could the organism be recovered after twenty-four hours. In the tonsillar crypts, the bacteria were no longer found after one hour in two cases out of four, and all four were clear before twenty-four hours. The pharynx was also cultured in the individuals receiving inoculations on the tongue and into the nose. The cultures indicated very little spread of organisms and no persistence in this region. These findings point to the presence of an effective mechanism for the disposal of organisms in the upper air passages. The author next gave his attention to the study of this protective mechanism. The lacrimal secretion he considers in no way bactericidal. In the nasal passages, the secretion is scanty, but here the backward sweeping of the ciliated epithelium is to be considered as well as the peculiar structure of these air passages, and the author believes that other than just

at the anterior nares, no permanent nasal flora exists. The mouth and throat, on the contrary, offer a favorable site for bacterial growth, as has been frequently shown by the presence of a definite flora even in the presence of the best possible oral hygiene. The flushing action of the abundant secretions here is a large factor of safety. The author points out that test-tube experiments are not lacking to show the inhibitory action of saliva on a variety of organisms, while studies *in vivo* have not been reported. He performed a number of well controlled experiments, which seem to indicate clearly the inhibitory and bactericidal action of saliva on *sarcina lutea*. This action was quite rapid, and was independent of the effect upon bacteria normally present in the saliva. In brief, he found that cultures made at intervals up to twenty-four hours from suspensions of *sarcina* in saliva yielded rapidly decreasing numbers of colonies of *sarcina*. The number after fifteen minutes was much reduced, only an occasional microorganism could be found after one hour, and none after two hours. The reaction of the saliva had apparently no influence, as the *sarcina* were readily grown in media of a slightly wider range of reaction than that found in the various specimens of saliva studied. There are a number of pathogenic bacteria which have been shown to flourish better in saliva than in broth, notably the pneumococcus. The meningococcus, too, has been found to grow better in media to which a little saliva is added. It would seem that the fate of *sarcina lutea* is well established by the present study, but how far inference by analogy may be carried is indeed debatable. The author promises further reports on other organisms.

Histological Changes in Squamous-cell Carcinoma of the Cervix of the Uterus after Radiation.—Justification for the use of radium in medicine can usually be determined by a more or less superficial examination. The exact problem in defining the effect of radium rays on normal and pathological tissue, however, requires a thorough understanding of both the radium and the malignant growth. Although many investigators have been impressed with the marked change in the relative amounts of parenchyma and stroma following irradiation, ALTER (*Jour. Med. Res.*, 1919, xl, 241) believes that the chronological sequence of the alterations in radiumized tissues is of utmost importance and cautions against drawing the generalized conclusions from an individual type of growth. In a series of 275 cases of squamous-cell carcinoma of cervix, ample opportunity was afforded to study several specimens from the same case representing different stages after radiation. The amount of radiation varied greatly, due to the proximity of application, but the error can be reduced to the minimum if a standard dosage with a varying time factor is assumed. The histological technic consisted in the judicious employment of various fixing and staining methods. The author calls attention to the fact that most cancers of the cervix arise from the basal-cell layer and are, therefore, non-keratinizing. Immediately after radiation, there is a latent period, the duration of which varies and cannot be determined without experiments. The earliest changes are inflammatory in nature and consist in an extensive eosinophilic infiltration as well as the formation of many

young, engorged blood channels with free hemorrhage and edema. After the first week, definite changes in the tumor cells occur and remain dominant. Both the nuclei and protoplasm swell, the former becoming uniformly pyknotic and their staining affinity changing from basophilic to acidophilic. A progressive vacuolar degeneration along with the eosinophilia, suggests profound chemical destruction. The tissues nearest the radium suffer first and, depending on the treatment, may resume malignant activities or proceed to more advanced retrogression. After continued radiation, mitotic figures disappear, usually in the second week and the stroma begins its ever-increasing advance, at first becoming diffuse so that the carcinoma really resembles a sarcoma. Later, the parenchyma is split into irregular islands by bands of cellular, young connective tissue. From the third week onward the chromatin substance suffers markedly, until, with dispersion of the nuclei it forms irregular globules and a diffuse mesh-work. About nine weeks after radiation, groups of peculiar, foamy, chromatin bodies occur in the stroma which increases in amount with a consequent decrease in the parenchyma. The author calls especial attention to the primary destruction of the tumor cells by the radium rays and the secondary increase in the connective tissue, which, while never actively proliferating, increases in volume, later only to contract into the usual collagenous or hyaline scar tissue.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Health Activities in Colleges and Universities.—SUNDWALL (*Public Health Reports*, No. 45, xxxiv, 2489) gives the following as a summary of an exhaustive treatment of the subject: (1) *Aims*: The University Health Service endeavors to be a most potent factor in reducing to the very minimum that large annual academic and economic loss which is due to the indisposition and illness of students. Further, its aim is to help each student entering the university to possess a healthy, vigorous, active and harmoniously developed body. The University Health Service stands for positive health. (2) *Activities*: There are three main divisions to its activities: (a) Personal attention, (b) sanitation, and (c) education. (a) The personal division is concerned with the physical examination of all students. Complete physical records should be kept. From each record can be determined in a large measure, just what procedure is necessary to keep the student in the best physical condition

during his academic life. The following are some of the branches of the work in the personal division: (i) Provisions for maintaining the health of the normal, healthy student by means of proper exercises, etc.; (ii) protection of the physically sound student from communicable diseases that are constantly creeping into the university, by the early detection and isolation of all cases of communicable disease—tuberculosis, typhoid fever, smallpox, scarlet fever, mumps, measles, etc.; (iii) provisions for the care and treatment of all such cases of communicable diseases; (iv) reconstruction-reclamation; correction of defects, advice and treatment to all subnormals; (v) advice to and treatment of all ill students. (b) Division of Sanitation: The students' environment must be made as hygienic as possible; hence this division concerns itself with the sanitary conditions affecting the student both on and off the campus. (c) Education: Finally, every student in the university must be made familiar with the elements of personal and public hygiene. Education in these important matters is carried on by means of courses in these subjects, daily bulletins, exhibits and lectures.

Determination of Bacteriotropic Content of Antimeningococcic Serum.—EVANS (*Public Health Reports*, No. 43, xxxiv, 2375) suggests that inasmuch as the pathology of cerebrospinal meningitis indicates that the bacteriotropins are concerned in the defense of the body against the meningococcus, the determination of the content of these antibodies in therapeutic serums should be of more value than the estimation of agglutinins and complement-fixing antibodies. A grouping of meningococci in accordance with bacteriotropic determinations is given, and it is shown that there is a fair correlation of these groups and the groups established by agglutination reactions. The content of the various antibodies in different serums does not always run parallel, and the same is to be said with respect to the loss of antibodies through the operation of unfavorable influences. The test is regarded as a valuable one for the testing of commercial serums.

Field Experiments in Malaria Control.—ROSE (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1414) states that for the average town in our Southern States having a thousand or more inhabitants and a reasonably high infection rate, malaria control by antimosquito measures is economically feasible; it is, in fact, a sound business investment. In heavily infected regions, in which the cost of mosquito control would be prohibitive, the amount of malaria may be greatly reduced by resort to screening, to immunizing quinin, or to destroying the parasites in the blood of the human carriers. The indications would seem, in fact, to justify the hope that by the systematic application of these measures the malaria in a community may be held within reasonable bounds, and that this result may be accomplished within limits of cost that the average community may well afford. The people in these communities are prepared to provide the funds by public taxation for malaria control when they have been shown by demonstration that the program proposed will accomplish definite results that justify the expenditure. The results thus far accomplished would seem to justify continuing these field experiments until the principal procedures that have been found useful in controlling malaria have been pretty thor-

oughly tested separately and thus evaluated. It will then be possible to operate intelligently a combination program in which each control measure will be given its place and will receive varying emphasis from time to time according to the local conditions that have to be met. This freedom in the use of our tools will in turn contribute toward the object that we have in view, namely, the highest degree of malaria control consistent with a reasonably low per capita cost.

The Ultimate Seasonal Infection of Malarial Fever, with the Mosquito Carrier as the Indicator.—MAYNE (*Public Health Reports*, 1919, xxxv, 1969) believes that by the dissection of mosquitoes and the detection in this manner of those carrying malarial parasites it is possible to apply measures of protection more intelligently than otherwise. The following from the "Discussion and Summary" indicates the field of usefulness of the measure: "Protection against malarial fever through prophylactic means, afforded by a knowledge of the presence of infective organisms in the mosquito, is a measure placed at the disposal of the sanitarian. This is offered through biological research, using the insect host as an indicator. There is a date (differing for place and year) up to which time mosquitoes are infective and beyond which time they are not. After this date malaria is not contracted by man. A knowledge of terminal infection with the mosquito as an indicator has considerable sanitary value, and it can be applied in a practical way by using it as a guide in deciding on the discontinuance of sanitary protection at a time when the mosquito no longer plays a pathological role. It furnishes the basis for the determination, in a selected zone, of a time when it is safe to curtail sanitary-control measures. Thus, needless expenditures of public funds may be averted in such cases where such funds are limited to malaria control—where it is not the purpose to eradicate the mosquito merely as a pest. Applied practically, this indicator would operate in this manner: Assuming that November 1 was the date determined as that of ultimate mosquito infectibility, and it was desired to recommend the safe time at which to discontinue oiling or other larvicidal measures, allow eighteen days for complete transformation from the larval stage, and twelve days for the adult mosquito to become infective, a total of thirty days to be counted back from the date of ultimate infectibility. The date to be named for the safe discontinuance of operations against the mosquito as an infecting agency would then be October 1.

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ORIGINAL ARTICLES

THE PHYSICAL SIGNS OF FOREIGN BODIES IN THE BRONCHI.¹

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THROUGH the kindness of my colleague, Professor Chevalier Jackson, an opportunity has been given to study the physical signs in a considerable number of patients with foreign bodies in the bronchi. This study is a discussion of the clinical aspect of some of the problems presented. No attempt is made to discuss the other phases. Dr. Jackson has done this in various publications, and a summary of many of the points can be found in a recent article.²

The study of these cases suggests a number of clinical problems: (1) How frequent is the occurrence of foreign bodies in the bronchi? (2) What symptoms and signs are there which are diagnostic or suggestive of their presence? (3) Is there any clinical picture or are there physical signs suggestive of the presence of a foreign body in the absence of roentgen-ray findings? (4) Are there definite physical signs suggestive of a particular kind of foreign body? (5) To what extent can we reduce the chance of error in failing to recognize the presence of a foreign body in a bronchus?

It is evident that we have to discuss very different sets of conditions, and that no one description can cover all the cases. Thus

¹ Read at the meeting of the Association of American Physicians, June, 1919.

² Jackson, Chevalier: Observations on the Pathology of Foreign Bodies in the Air and Food Passages, Surg., Gynec. and Obst., 1919, p. 201.

we have certain signs due to the foreign body and the local reaction set up by it, and others due to changes in the lung supplied by that bronchus. The character of the foreign body is important; a safety-pin may do little damage while a peanut causes marked changes very rapidly. One foreign body plugs a bronchus completely, another acts as a ball valve. Pus forms below the foreign body and may be retained or escape. The secretions may be forced into bronchi other than the one involved, or from the affected lung into the bronchi of the opposite one, so that signs are found on both sides. The signs may change greatly from hour to hour in acute cases so that any set description fitting all cases is out of the question.

1. THE FREQUENCY OF FOREIGN BODIES IN THE BRONCHI. It is quite impossible to give any statement on this point. In the Jefferson Hospital material they are comparatively common, but this is exceptional, as the patients come from all parts of the United States and Canada to consult Dr. Jackson. Two things suggest that such cases are more common than we have generally supposed. One is the number of patients who come with a history which shows that for months or years a foreign body has been present and unsuspected and the other is the number of patients from the near neighborhood with a foreign body, but without suspicion of it on their part. The roentgen rays have aided greatly in the recognition of certain foreign bodies, but there are substances which do not show in a roentgen-ray plate, and it is for the recognition of these that a study of the physical signs is particularly important. Certainly, the impression has been strongly forced upon me that the condition is much more common than the majority of us have suspected and my memory brings up cases seen in the past in which the presence of a foreign body was probably overlooked.

One point deserves emphasis in this connection—the history. Most of us would suppose that there would be small chance of a foreign body passing into the trachea and then to a bronchus without marked acute symptoms which could not fail to be noticed. We must realize that this is not necessarily the case and that fairly large bodies may reach the bronchi without any acute symptoms. For example, in one case (No. 611³) there was no definite history as to when the foreign body, which was an atomizer tip, had been aspirated. The patient knew nothing of it, but on searching his memory remembered that about eighteen months before a tip had disappeared. This particular patient had been thought to have tuberculosis. At the time of writing this paper a boy of eight years of age is under observation. He was sent to the clinic for some laryngeal condition and examination shows part of a collar-button in a bronchus. No history can be obtained of any acute

³ The numbers are those in Dr. Jackson's series, and are given to identify the cases when reported elsewhere.

onset and there is no clue as to the time of aspiration. Such cases emphasize the need of caution in concluding that the introduction of a foreign body must cause some symptoms or disturbance which can be noted. This point cannot be too strongly emphasized.

My impression is that these unrecognized cases of foreign bodies in the bronchi are by no means rare. Naturally the greatest difficulty arises in the instances in which the body cannot be recognized by the roentgen rays, probably in from 10 to 15 per cent. of all cases. There are two sharply defined groups of unrecognized cases. The first is that in which the body sets up a very acute inflammatory process and death follows in a short time—the diagnosis of pneumonia usually being made. This is particularly likely to follow the aspiration of some variety of nut, especially a peanut, by a young child, and how many of these cases occur we have no means of knowing. The younger the patient the more acute this process usually is and in such cases it is evident that the history is often not complete. The other group is that in which marked changes are set up and the symptoms become chronic, a diagnosis of pulmonary tuberculosis or bronchiectasis being made. In such a case in an adult seen some years ago there were marked signs over the lower right lobe. We suspected the possibility of a foreign body but there was no history to suggest it and repeated roentgen-ray examinations did not aid. After eighteen months of illness she coughed up a small piece of bone. This was followed by rapid recovery.

2. CLINICAL FEATURES CAUSED BY FOREIGN BODIES. The greatest possible diversity occurs as the signs vary markedly. A safety-pin, particularly if closed, is not likely to cause much change in a short time while a screw or tack which plugs a bronchus results in rapid changes. One substance may plug a bronchus or set up inflammation which does the same thing, and another may entirely plug a bronchus at one time and a little later allow air to enter past it, so that it is evidently impossible to give any exact account of the signs. The foreign body is more often on the right side and has a tendency to go to the bronchi supplying the lower lobes.

The change in the signs in a short interval is a striking point. In some cases this is apparently due to a change in position of the foreign body, in others air may enter at one time and not at another. Thus in one patient the signs suggested collapse of the involved lobe and a few hours later it was apparently overdistended, suggesting a valve action of the foreign body. The amount of secretion and the effect of coughing on its expulsion may cause rapid changes in the signs. The signs may be local or general; it is not uncommon to find signs over both lungs. Emphasis should be placed on this point, as in some cases the signs are more diffuse on the unaffected side. This may lead to serious error and appears most likely to occur in the younger patients.

There is only one sign which has been present in every patient seen by me, and that is *decreased expansion* of the affected side. It may be the only sign present, as in the following case:

No. 697. The patient was a woman, aged thirty-two years, who, two weeks before, coughed while holding a safety-pin in the mouth and aspirated it. She felt some soreness in the throat, followed by a tickling sensation and a hacking cough. Two days later she had more severe coughing, followed by pain in the upper right chest. On admission she complained of slight cough and pain in the *right* side of the chest. On examination there was *only one sign* to be found—diminished expansion of the *left* side. The percussion note and the breath sounds were clear. No rales were heard. In view of this the opinion was given that the foreign body was on the left side, but that there was no clue to its position beyond that. The roentgen ray showed an open safety-pin in the left bronchus without any evidence of a pathological process in the lung beyond the pin. Dr. Jackson removed the pin and three hours afterward the expansion was absolutely equal on the two sides.

In some cases it has been possible to hear rales, which may be described as rather characteristic, over a small area. In each case in which they have been observed the foreign body was metallic, but the cases are too few to draw any positive conclusions. These particular rales may be described as very fine and softer than the early crackling rales heard in lobar pneumonia. They may be compared to the crackle made by very fine tissue paper. In the two cases given there was no other evidence of any change in the lung tissue made out by physical or roentgen-ray examination.

No. 683. The patient was a girl, aged eighteen years, who was having some dental work done on December 23, 1918. A dental root-canal reamer was placed in the tooth and the dentist turned to get another instrument. The patient felt the reamer slip out of the tooth and lodge on the tongue. She tried to take hold of it, but it disappeared. She had a paroxysmal attack of coughing but did not feel any sensation of a foreign body in the throat or air passages. Two days later she took ill with what was regarded as an attack of influenza, with which she had a severe cough and considerable sputum. After this she was very weak and had some cough, which was slightly productive. She complained of an occasional sharp shooting pain in the lower left thorax, which seemed to be brought on by coughing. On admission on January 31, 1919, examination showed slightly less expansion of the lower left thorax. The percussion note seemed equal on the two sides. The breath sounds were very feeble on both sides, and this seemed to be rather more marked over the lower left lobe. In the lower left axilla there were very fine crackling rales, which

seemed to come from a distance. They were heard mostly at the end of inspiration and were slightly more marked on deep breathing, but were never loud. There were no definite signs of any solidification in the lung tissue. The roentgen-ray study showed the foreign body in the left lower lobe bronchus. There was no evidence of change in the lung beyond it. The reamer was removed on February 1. Dr. Jackson found the trachea very red and inflamed. The left bronchus showed a high degree of inflammation, with adherent masses of thick secretion which surrounded the foreign body, part of which was in the posterior branch of the left inferior lobe bronchus.

It is certainly surprising that there were not more signs with this degree of change in the bronchus. Two days later there was still slightly less expansion of the lower left side and a very few of the fine, crackling rales could be heard on deep breathing.

No. 690. The patient, a man, aged fifty-six years, was seen on March 15, 1919. On March 7, while standing on a ladder holding a staple in his mouth, he endeavored to answer a question and aspirated the staple. He did not have any symptoms at the time. The next day he complained of tickling in the throat, and a roentgen-ray examination was made which showed the staple in a bronchus. An attempt at removal was made (in another place), but was not successful. At the time of examination the patient stated that the roentgen ray showed the staple in the *left* lung and pointed to the third left interspace as the spot where he felt it. The importance of not accepting a patient's statement as accurate was shown by the examination. This was complicated by the fact that he evidently had old trouble on the right side, and he stated that he was thought to have had tuberculosis in youth. The right shoulder was lower, there was less expansion, the right scapula was longer and moved less, and there was dulness, with harsh breath sounds at the right apex. The percussion note was equal in the two axillæ, but in the lower right axilla there were fine rales at the end of inspiration heard over a small area. These seemed to come from a distance and were extremely fine. They were the same as those heard in case No. 683. No rales were heard on the left side. Despite the positive statement by the patient that previous roentgen-ray studies had shown the staple in the left lung and that he could feel it there, these rales suggested that it was in the right lower lobe bronchus. The roentgen-ray study (Dr. Manges) showed a metal staple in the main bronchus of the lower right lobe and very little pathology in the lung below the staple. Dr. Jackson found the staple in this situation and removed it. The fine crackles were heard unchanged three hours after the removal, but had disappeared the following day.

One hesitates to give too much importance to these rales, but they are different from rales which I have heard in any other condition,



FIG. 1.—Case 690. Staple in right lower lobe of bronchus. Little change below the foreign body.

and have only been heard in cases in which the foreign body was metallic in character. They are certainly worth keeping in mind,

but it is well to state that very careful listening is required to hear them. They might easily be missed in a hurried or perfunctory examination.

The next stage of the development of the signs is found when changes have occurred in the lung. An example is as follows:

No. 684. This patient was a boy, aged three years, seen on January 31, 1919. The history was that on December 21, 1918, it was noticed that the patient had something in his mouth which was suddenly aspirated. A severe coughing attack followed and the patient was blue for a time. In the next two or three days repeated coughing attacks occurred and there was a slight elevation of temperature. The patient was attended by a physician who made a diagnosis of influenza and later of pneumonia on the left side. During this time the patient seemed to be very ill and had fever, which occasionally reached 104° , with very severe cough and considerable pain in the left side of the chest. Examination was difficult, as the child was crying constantly and was very restless. The expansion was diminished on the right side. The percussion note was clear and hyperresonant on the left side, but on the right side there was some impairment on percussion throughout, slight in the upper part and most marked in the lower right front, axilla and back. The breath sounds were clear throughout the left side and not a single rale was heard. On the right side, on quiet breathing, expiration was not heard, but was distinctly audible when forcible expiration was made. In general the breath sounds were distant over the right side. In the upper part of the right chest the breath sounds were rather higher pitched than normal, but were not tubular. There were many coarse, crackling rales in the lower right interscapular region and a certain number in the lower axilla. After forcible coughing the rales changed somewhat, becoming rather fewer. There was no wheeze heard. The signs suggested that the foreign body was in the lower right bronchus. Dr. Jackson removed a machine screw from the right inferior lobe bronchus. Large amounts of pus escaped during the operation and were coughed up subsequently.

It is interesting to note how frequently the diagnosis of pneumonia is made in these cases. This comes out very frequently in the histories, but a careful study of the physical signs should prevent this error. Fever is very common after the aspiration of a foreign body, and if there is dyspnea, with cough and bloody or blood-streaked sputum, the diagnosis of pneumonia is suggested before the examination of the thorax is made. Decreased expansion on one side and dulness may suggest the diagnosis, but a careful study of vocal fremitus and the auscultatory signs should show that if the condition is pneumonia there is plugging of the bronchus—a rare

condition. The writer has not seen pneumonia associated with any case of foreign body in a bronchus. The local signs are usually those

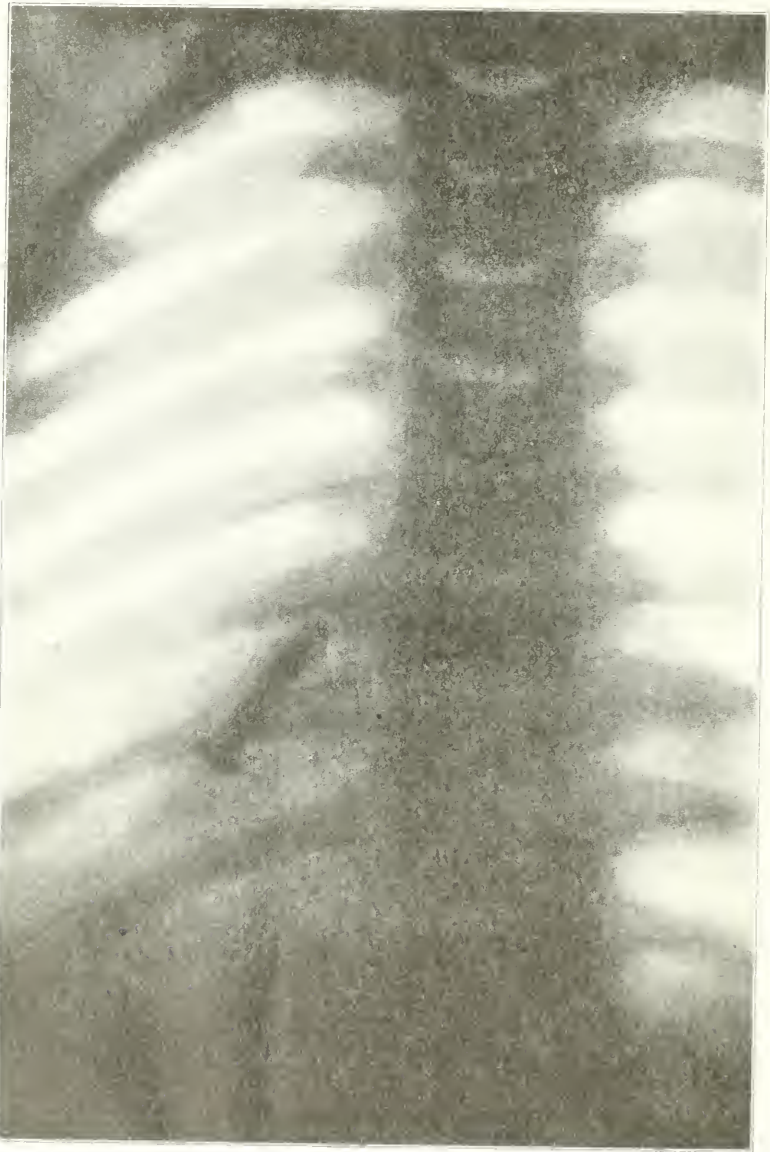


FIG. 2.—Case 684. Foreign bodies in bronchi.

due to the supplying bronchus being obstructed. Variations depend on the quantity of air in the portion of lung, the amount of

secretion and the persistence and completeness of the plugging of the bronchus. In many cases there are no breath sounds or rales heard over the affected parts, in others there may be rales but no breath sounds. In the majority the affected portion of lung seems to be airless and in the roentgen-ray plates at early stages shows as a homogeneous shadow. Later fibrosis, abscess formation and bronchiectasis may be found. These show no special peculiarity in the physical signs, but are important in that they may be wrongly diagnosed as tuberculosis.

"ASTHMATOID WHEEZE." This term has been employed by Chevalier Jackson to describe a sign which is present in a considerable number of cases of foreign body in the trachea or bronchi. He has discussed it in considerable detail in a recent article.¹ This sound can be heard by placing the ear or the bell of the stethoscope close to the patient's mouth. It may be heard with both inspiration or expiration, but sometimes is only audible at the end of forced expiration. Forceful respiratory effort usually increases the loudness and intensity. It differs from the wheezing sounds heard with bronchial asthma, but this difference is difficult to describe in words. The "wheeze" varies in pitch and loudness, depending on the character of the foreign body causing it. In no case in which the writer observed it could the sound be heard over the chest wall. In some cases the sound comes and goes without any explanation being evident. The report of a case in which it was very marked is as follows:

No. 675. The patient, a white male, aged forty-four years, was admitted on December 20, 1918, complaining of cough and shortness of breath. Four days before admission a dentist was fitting a gold bridge, when it slipped back in the mouth and was aspirated. Following this there was a paroxysm of coughing and the patient had a momentary sensation of a foreign body in the throat. The same evening he had an attack of dyspnea, which lasted for about half an hour and which he compared to asthma. With this there was an unproductive cough. With the coughing he had noted a certain amount of wheezing. On examination on December 21, 1918, the patient was propped up in bed. He had slight dyspnea but no cyanosis. On listening with the ear near the patient's mouth a wheezing sound was heard, most marked with inspiration and very slightly heard with expiration. It seemed to be rather more marked when he took a deep breath. Expansion was much less over the lower right chest. On percussion there seemed to be slightly less resonance on the right side which was most marked in the lower right axilla and back. The breath sounds in general, were rather harsh and this was more marked on the

¹ AM. JOUR. MED. SC., 1918, clvi, 625.

right side. No rales were heard on the left side, but there were a great many over the whole of the right lung. They were of very variable character, the majority whistling and groaning, and some with rather a wheezing character. The roentgen rays showed an artificial dental plate, apparently composed of three teeth in the right upper bronchus. Removal was done on December 21, and immediately after it the wheezing sounds heard at the mouth disappeared. Two days after removal expansion of the two sides of the chest seemed absolutely equal, percussion was clear, no rales were to be heard and the breath sounds seemed to be equal on the two sides.

This sign appears to be of considerable value, particularly in the cases in which the foreign body does not show in the roentgen-ray plate. It has been observed in many cases and occurs with different substances. It should be listened for in all cases of obscure thoracic diagnosis in which the presence of a foreign body has to be considered.

Certain foreign bodies set up very acute and dangerous changes, among which the *peanut* takes first place. It sets up a rapid and severe reaction and the younger the child the more severe this is. The following is an example:

No. 682. The patient was a boy, aged five years, who on December 20, 1918, choked while eating peanuts. There was much coughing and gagging, with cyanosis at the time. Later the symptoms subsided, but in the evening the father noted that there was a wheezing sound at intervals, with a dry cough. Until January 7, 1919, the patient seemed well and played as usual. On this date the cough increased in severity and there was severe dyspnea, but the wheezing ceased. The physician said that air was not entering the left lung. On January 14 an attempt was made to do bronchoscopy (in another city), but without success. The patient was admitted to the Jefferson Hospital on January 16, 1919. On examination he was comfortable and showed neither distress nor cyanosis. Over the right side there were harsh breath sounds, with many medium and coarse rales. The left side of the thorax showed decided fulness, but no expansion. Vocal fremitus was difficult to obtain, but seemed much decreased. The percussion note had a curious quality of tympany, with an element of dulness. The breath and voice sounds were not heard over the left side. No rales were heard. The heart was not displaced. We considered that the peanut had acted as a ball valve and allowed air to enter but not to escape. The roentgen ray confirmed this, and after the removal of the peanut showed an equal amount of air in the two lungs.

The larynx was found to be much swollen and the trachea greatly inflamed. There was pus coming freely from the right

main bronchus. The left bronchus was intensely red and swollen and contained tenacious pinkish pus. After sponging this away the peanut was seen in the left bronchus. It was removed without crushing. After removal the left side still showed decreased expansion, but harsh breath sounds could now be heard, with many loud bubbling rales. Within four days the child felt well and the signs in the chest had nearly cleared. There was still less expansion, with the percussion note and breath sounds about normal.

This case illustrates one point which may cause error—the presence of signs on both sides. This is usually due to secretions from one side being forced or carried over to the opposite bronchus. Occasionally a foreign body may be moved from one side to the other, or, in the case of a nut portions may be broken off and carried over. It may be said, however, that there is rarely any doubt of the side involved if a careful examination is made. The decreased expansion is the most important guide in deciding this point. Special reference must be made to the need of care in the peanut cases, as a general process is set up in both lungs and the roentgen-ray plate may show more pathological changes on the side which does not contain the nut.

To this condition the term *Arachidic Bronchitis* has been applied by Jackson and Spencer.⁵ They apply this term to the condition set up by the presence of a peanut in the respiratory tract, but other nuts give much the same symptoms. The clinical picture is rather a distinctive one associated with an edematous, purulent tracheobronchitis which often results in lung abscess. The cases appear only in children and the symptoms come on rapidly, with high fever, severe toxemia and marked thoracic signs. The dyspnea is extreme, cyanosis is usually marked and there may be a purulent tenacious sputum. The fever is usually irregular, but is high for part of the day. The signs are general and are those of an intense general bronchitis, with a great variety of rales, the majority coarse and bubbling. There is decreased expansion on one side as a rule, but if portions of the nut are on both sides, as sometimes happens, this does not hold. Depending on the size and situation of the particles there may be dulness and absence of breath and voice sounds if a bronchus is plugged. The lung supplied by the plugged bronchus contains much secretion and has been described as "drowned lung." This is often mistakenly regarded as representing pneumonic consolidation. The "asthmatoïd wheeze" is present in a majority of the cases. The voice is usually lost.

"We should always remember the possibility of peanut bronchitis when consulted regarding a child who rather suddenly develops irregular fever, restlessness, dyspnea with cyanosis, paroxysmal

⁵ Jour. Am. Med. Assn., 1919, lxxiii, 672.

cough and the signs of a diffuse, generalized bronchitis, attended with wheezing respiration. A history of choking on a peanut, or of eating peanuts at about the time of inception of the illness, renders the diagnosis almost certain." (Jackson and Spencer.)

3. As regards the question of distinctive signs of foreign bodies one speaks with great hesitation. The two signs mentioned certainly deserve careful study, namely, the presence of the fine "tissue-paper" rales over a small area and the "asthmatoïd wheeze." The former has been observed with small metallic bodies only, but further observations may show that it occurs with others. They are not necessarily present in every case of small metallic bodies. The "wheeze" seems to offer more as a suggestive sign; Dr. Jackson has now observed it in over 50 cases, so that it seems to be of much importance. I venture to suggest the value of keeping it in mind and noting its presence or absence in doubtful cases.

In the very acute cases, usually due to some substance such as a nut or burr, the marked general signs may be of value, especially if there is any history. The problem is complicated by the presence of fever, which may be high, and the general picture of an acute infection. Some of these patients present a picture of the most intense toxemia. A general picture suggestive of a severe bronchopneumonia, but without any positive physical signs of it, should excite suspicion of something else.

The occurrence of signs in a lower lobe for which there is no evident explanation should always suggest the possibility of a foreign body. The same may be said to be true of local signs anywhere the etiology of which is not clearly proved.

4. As regards physical signs suggestive of a particular kind of foreign body, in the absence of a positive history one hesitates to speak with any certainty. One might *suspect* but it seems difficult to be *sure*. Evidently this is most important in the cases in which the roentgen rays give no aid. In such instances the acute general signs caused, for example, by a peanut are perhaps as suggestive as those of any group.

5. THE REDUCTION OF ERRORS IN DIAGNOSIS. It is evident that errors will be fewer if the possibility of a foreign body is considered. Too often it is not thought of and a hasty examination, soon after the entrance of a foreign body, results in a careless diagnosis, usually of pneumonia, which is not revised. This seems the only explanation when the changes due to a foreign body are diagnosed as tuberculosis, and this is accepted for years. In general, foreign bodies tend to go downward and set up changes in the lower lobes. It seems to take a great deal of telling to convince some of us that tuberculosis at the base of a lung alone is very rare. In every case of basal involvement, in every case of abscess and of bronchiectasis the possibility of a foreign body should be considered.

In the acute cases, typically illustrated by the reaction to a

peanut, the problem may be more difficult, but the suggestions given by Jackson and Spencer are an aid. The picture is in some ways like a very acute severe bronchitis with bronchopneumonia, but it reads more like it in the description than it looks like it in the patient. It is one of the differences which is difficult to state in words, but is suggested at once after one has seen the patients. The intense toxemia, marked dyspnea and cyanosis, and high fever without any signs of pneumonia, are points to be noted.

SUMMARY. 1. Cases of foreign body in a bronchus are not mere curiosities but are more common than we have supposed.

2. There may be no disturbance at the time of entrance of a foreign body and no suggestion in the history of such a happening.

3. Certain signs are of value, especially decreased expansion on the affected side, the presence of very fine rales and the "asthma-toid wheeze."

4. Some foreign bodies, such as a peanut, set up a very acute general process which is fairly distinctive. Other structures, such as metallic objects, cause permanent changes, usually in a lower lobe.

5. The chief errors in diagnosis are to mistake the signs for those of pneumonia in the early stages and in the acute cases, and for tuberculosis after the body has been present for some time.

THE OCULOPUPILLARY FIBERS OF THE SYMPATHETIC SYSTEM: DIVISION OF THE FIRST THORACIC ROOT IN MAN.¹

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It is surprising that so little is known regarding the course of the sympathetic fibers in the brain; especially is this true of the cerebrum. We have evidence as to the location of the oculopupillary fibers of the sympathetic system in the cervical cord, medulla oblongata and pons, but scarcely anything is known of these fibers in their relation to higher parts of the brain. My attention has been directed at this time only to the oculopupillary fibers of the sympathetic system. Paralysis of these fibers produces the Claude Bernard-Horner syndrome. It is not definitely known that this paralysis occurs with hemiplegia of cerebral origin, but a case in which it seems to have so occurred has come under my observation and has led to investigation of the literature bearing on this subject.

¹ Read before the Philadelphia Neurological Society, November 21, 1919.

W. C., aged eleven years, was examined October 30, 1919.

When six months old he had a series of convulsions. The attack lasted about two weeks. When he began to walk at two years of age his mother noticed that he was awkward and could not use his left arm and hand and that the left leg was weak. Between the ages of six months and two years his mother said he was "helpless," *i. e.*, he was not as active as other children. At the time of examination he had been in school five years, was backward and was only in the second grade.

He had left hemiplegia, implicating also the face. The tendon-jerks were exaggerated on the left side and the Babinski reflex was present on the left side. The left pupil was smaller than the right and the mother was unable to say how long this difference had existed, but evidently it had been present a long time. The left palpebral fissure was smaller than the right. Ocular movements were normal. The left upper and lower limbs were not as well developed as the right. The tongue when protruded deviated to the left. The left foot was in the position of talipes equinus.

Dr. H. M. Langdon reported on the examination of the eyes. Vision: O. D., 6/12. O. S., 6/12?? Right palpebral fissure 10 mm., left $7\frac{1}{2}$ mm. Right pupil 3 mm., left $2\frac{1}{2}$ mm. Exophthalmos, right eye, 14 mm., left $13\frac{1}{2}$ mm. Ophthalmoscope showed disks oval, good color, with no fundus changes.

There was evidently a paralysis of the cervical sympathetic on the side of a long-standing hemiplegia, as shown by the small pupil, small palpebral fissure and retracted eyeball. No evidence of injury of the neck and no enlargement of the thyroid gland causing pressure on the cervical sympathetic could be found. There was no cranial nerve palsy suggesting a basal lesion. The lesion must have been above the lower part of the cerebral peduncles or some cranial nerve probably would have been involved. There is no evidence that the sympathetic palsy occurred simultaneously with the hemiplegia, but there was no other cause known than that producing the hemiplegia, and the mother could not state when the oculopupillary symptoms developed; they had been present a long time according to her statement.

In the discussion of this case Dr. S. D. Ingham, described a case in which he had made the diagnosis of a thalamic lesion, because of disturbance of tactile pain and thermic sensations, with spontaneous pain of unilateral distribution. Associated sympathetic symptoms consisted of a small pupil and narrow palpebral fissure on the affected side and unilateral sweating of the face and trunk.

Dr. Samuel Leopold also mentioned a case he had presented in 1916, in which right hemiplegia with Jacksonian epilepsy confined to the upper extremity was associated with oculopupillary symptoms.

Examination of the literature has revealed some interesting information. Karplus and Kreidl, by placing an electrode at the

base of the brain in the living cat, obtained important findings. The point of irritation was just behind the optic tract near the oculomotor nerve lateral to the infundibulum. Maximal dilatation of both pupils resulted from this irritation, with widening of both palpebral fissures. This result was constant in more than twenty cats, whether the animal was in a state of narcosis or not. A weak current was sufficient to cause the dilatation. When a very feeble current was used the effect on the heterolateral eye was always prompter than on the homolateral eye.

They demonstrated that this irritation was conveyed through the cervical spinal cord. The cervical sympathetic on each side was exposed. Irritation in the above-mentioned area of the base of the brain was then made to cause dilatation of the pupils. If after this irritation the heterolateral cervical sympathetic was cut, renewed irritation of the base of the brain caused no effect on the heterolateral side, while the effect on the homolateral eye was as prompt as it had been previously. If then the homolateral cervical sympathetic was divided the pupil of the homolateral side could not be influenced by basal irritation. These experiments were repeated, with the same results in a number of animals.

Electrical irritation of the dura, the cerebral hemispheres, the peduncles and the infundibulum was without effect.

When the intracranial portions of the trigeminal and oculomotor nerves and the optic tract were cut, irritation of this mentioned area of the base of the brain produced the same results as before. Removal of the cerebral hemisphere, even complete separation of all parts of the cerebrum from this irritated area, so that only a little of the cerebrum remained with the brainstem, did not disturb the effect of the irritation.

They concluded that irritation of the base is transmitted through the homolateral cerebral peduncle and crosses in part lower down to descend in the cervical cord, predominatingly in the heterolateral side and then through both cervical sympathetic cords to the eyes.

They did not know whether a center was irritated in these experiments, and if so possibly it was the corpus subthalamicum; or whether a tract near the surface was irritated, but they inclined to the view that a center was irritated. They proposed to study, further, the relation of their basal irritable zone to the cortex.

It seems probable from these experiments that sympathetic fibers for the eye exist in the cerebral peduncle in the cat and that most of these fibers supply the heterolateral eye.

In their second paper on this subject, Karplus and Kreidl stated that their experiments were made on dogs as well as cats. They believed the results obtained by them, even after removal of the cerebral mantle, prove that the irritable basal area is a center and not a place where sympathetic tracts come near the surface. They extirpated the cerebral hemisphere on the side in which they

irritated the basal part of the brain and they did not think it necessary to extirpate the contralateral cerebral hemisphere. They believed there was no indication of decussation between the cerebral cortex and the midbrain. In this second paper they demonstrated that a certain relation exists between the cerebral peduncle and the homolateral cerebral hemisphere and not the heterolateral hemisphere.

They determined by marking the irritable zone at the base and then making microscopic sections that their sympathetic center was in the hypothalamus near the dorsomedial portion of the foot of the cerebral peduncle, in the frontal part of the corpus subthalamicum.

They obtained similar results in the ape, but the effect on the contralateral sympathetic was even greater than in the cat.

They found that in cats they were able frequently to obtain by electrical irritation of one frontal pole of a cerebral hemisphere, with a weak current, bilateral maximal irritation of the cervical sympathetic. They then destroyed their basal sympathetic center on the side on which they had irritated the frontal lobe and were no longer able to obtain irritation of the cervical sympathetic cords by placing the electrode on the frontal lobe in the region from which they had previously been successful. Irritation of the corresponding spot in the other frontal lobe still produced irritation symptoms in both cervical sympathetics. This is further evidence that the basal area is a center.

In their second paper Karplus and Kreidl referred to the fact that v. Bechterew obtained the signs of irritation of the sympathetic to the eye by stimulation of the medial portion of the optic thalamus, but they stated he did not determine whether he stimulated a sympathetic center or a tract in the part stimulated. This experiment may have some bearing on the case reported by Ingham referred to above.

Karplus and Kreidl also reported in their second paper that stimulation of the sympathetic to the eye by pain depended on the hypothalamic center they described.

In their third paper from their experiments on cats they concluded that each half of the cervical cord conducts impulses from the brainstem to both cervical sympathetic cords. Decussation does not occur in the cervical spinal cord but below the cervical cord. They acknowledge that their results from cats are at variance with those of others from experiments on rabbits. I feel certain that in man the decussation of these fibers is not in or below the cervical spinal cord.

Different investigators have represented different parts of the cerebral cortex as suitable for electrical irritation of the cervical sympathetic, but Karplus and Kreidl used the frontal lobe. They believed it is certain that in the cat the hypothalamic region as

well as the frontal cortex sends impulses to both cervical sympathetic cords. The irritation of the hypothalamic region always affects the cervical sympathetic, but the irritation of the cerebral cortex in different parts is not always shown in the cervical sympathetic. They agree with other authors that there is no definite sympathetic center in the cerebral cortex, it is certain only that in many animals a feeble current may more readily cause irritation of the cervical sympathetic from certain parts of the cerebral cortex than from other parts. This is not a very elucidative statement and it is evident that very little is known of sympathetic fibers in the cerebrum.

Their work seems to establish the existence of an important sympathetic center in the hypothalamus, but there is still much doubt as to how the fibers from this center get to their point of exit from the spinal cord, certainly the doubt is very great as regards man. It would seem that in the cat the hypothalamic center has more control on the heterolateral eye than on the homolateral eye, and this influence is even greater in the ape than in the cat. Their work leaves us in doubt as to a decussation of oculopupillary fibers in the cerebral peduncles, but it indicates that there is no decussation of these fibers above the cerebral peduncles.

Trendelenburg and Bumke stated that extensive destruction of the cerebrum, especially of the frontal lobe, has been observed to cause a difference in the pupils, but findings are conflicting as to whether the homolateral or heterolateral pupil is contracted. They reported some experiments in which the entire cerebral mantle in cats and dogs was removed in order to determine the influence of the cerebral cortex over the sympathetic to the eye. In four experiments unilateral removal of the cerebral mantle caused slight homolateral narrowing of the pupil, but they did not determine whether this influence was exerted through the oculomotor nerve or the cervical sympathetic. The difference in size of the two pupils was slight, less than in unilateral section of the medulla oblongata or of the cervical spinal cord, and therefore they said that this control of the pupil from the cerebrum is not to be accepted unreservedly as transmitted through the cervical spinal cord on the same side. They believed the cerebral mantle has no essential influence on the control of the pupil exerted by the cervical spinal cord, as demonstrated by one of their experiments. Both cerebral hemispheres in a cat were removed, one after the other, and then unilateral section was made at the junction of the medulla oblongata and cervical cord. The homolateral pupil after the section of the cord became smaller, although before the section it had been a little larger. Their work therefore affords little evidence of the control of the cerebrum over the sympathetic fibers to the eye.

Bumke asserted that irritation of the sympathetic fibers to the iris from cortical conditions although much discussed, has not been

demonstrated, and such an occurrence is improbable. He stated that we do not know the origin of the sympathetic fibers for the eye, but that without doubt there is a relation of the cerebrum to the sympathetic innervation of the iris.

Oppenheim observed a vasomotor form of Jacksonian epilepsy, consisting of attacks of cyanosis of one arm and of the face on the same side as the affected arm, with or without unconsciousness. The cyanosis of these parts finally became persistent and was associated with myosis and narrowing of the palpebral fissure and paresis of the arm and face. The report of this observation is very brief and the context implies that the symptoms were all on the same side of the body, and the case is confirmatory of the findings in my case.

Oppenheim believed that certain of the sympathetic symptoms of the eye may be dependent on the cerebral cortex. v. Monakow stated that v. Bechterew reported a case in which the right pupil could be dilated voluntarily almost to the maximal degree. The dilatation persisted after the impulse had ceased and disappeared after winking. v. Bechterew cited another case in which both pupils could be dilated voluntarily. v. Monakow believed these observations demonstrate that a close connection exists between the cortex and the center for the dilatation of the pupil.

I have come to the conclusion that in man the oculopupillary fibers do not decussate, or at least in very slight degree, in the pons or below this in the medulla oblongata or cervical cord. In two cases of tubercle of the pons, which is a lesion destroying the axis-cylinders where it exists and not permitting them to pass through as does glioma, the oculopupillary symptoms were on the side of the lesion. I have repeatedly seen oculopupillary paralysis of the sympathetic on the side of the lesion resulting from occlusion of the posterior inferior cerebellar artery. This occlusion produces softening in the lateral part of the medulla oblongata. It is possible that the sympathetic fibers decussate in the cerebral peduncle, but the evidence of this is far from conclusive.

In the case of tubercle of the pons reported by Potts and myself the pupil was small on the side of the lesion. The left side of the pons was much larger than the right. In its upper part, just above the entrance of the fifth nerve, a tumor was found occupying the left half of the tegmentum and invading a little the pyramidal tract on the same side. In the lower part of the pons the tumor implicated the left middle cerebellar peduncle and the pyramidal fibers on the left side, but did not invade the dorsal part of the tegmentum. The right side of the pons was not encroached upon by the tumor at any part. The nucleus of the sixth and probably that of the seventh nerve escaped, but the fibers of these nerves within the pons must have been compressed by the tumor. In this case the pupils were unequal, the left being the smaller, *i. e.*, the small pupil was on the side of the lesion confined to the pons.

In another similar case studied and reported by me the same relations existed. A tubercle was found in the left side of the pons. The left cerebral peduncle was larger than the right and the tumor extended into the lower part of the left cerebral peduncle. In the middle portion of the pons it invaded slightly the right side of the pons. The left pupil was 2 mm. in size and the right 3 mm. in size. Both pupils reacted to light and in accommodation and convergence. Under homatropin the right pupil was dilated to 6 mm., the left to $4\frac{1}{2}$ mm. Here also there was sympathetic paralysis on the side of the lesion in the pons and homatropin dilated the left pupil considerably less than the right. From these two cases it seems that the sympathetic fibers of the eye may be paralyzed by a lesion of the pons and that these fibers do not decussate in or below the pons.

There is scarcely any doubt as to the point of exit of the oculopupillary fibers from the spinal cord. The work of Claude Bernard and later that of Mmes. Dejerine and Klumpke have established the fact that these fibers must leave the cord by the first thoracic root, and possibly by the eighth cervical and second thoracic roots, and probably through the anterior divisions of these roots. While this determination has been made by experiments on animals and clinical observations on man, there is no case recorded, so far as I know, in which the first thoracic root alone was divided in man at operation and the resulting paralysis determined. The opportunity of determining the paralysis and the oculopupillary symptoms following division of the first thoracic root has recently been given me. At an operation for removal of a tumor of the cord it became necessary to divide this root on one side in order to excise the tumor. Oculopupillary symptoms had not existed previous to the operation, but they became very pronounced following the operation.

In the Klumpke paralysis oculopupillary symptoms form an essential part of the clinical picture. Dejerine describes the Klumpke type of paralysis as follows: It usually is preceded by a total radicular brachial plexus palsy. It assumes the form of ulnar palsy and implicates the small muscles of the hand, the thenar and the hypothenar eminences and the interossei muscles. Anesthesia of radicular type implicates the internal half of the hand and the forearm, *i. e.*, it is in the zone of cutaneous distribution of the ulnar and internal cutaneous nerves. Associated with this are myosis, narrowing of the palpebral fissure and retraction of the eyeball. She attributes the symptom-complex to a lesion of the first and second thoracic roots or of the eighth cervical and first thoracic roots.

Mmes. Dejerine and Klumpke found in sectioning the roots of the brachial plexus in the dog that only the division of the inferior roots, and especially of the first thoracic root, caused oculopupillary phenomena. Division of the eighth cervical, and especially of the

first thoracic root, made near the vertebral column, produced the same oculopupillary signs. These signs occurred in her experiments only when the first thoracic root was divided, but the eighth cervical also was divided.

In quoting Claude Bernard she states that his experiments first showed (1862) that the oculopupillary fibers pass by the first and second thoracic roots, but the predominance of the first thoracic in the symptom-complex was recognized by him. Her own experiments showed that division of the nerves of the brachial plexus causes oculopupillary phenomena only when the first thoracic is implicated. It does not seem to be possible from these experiments to exclude the eighth cervical and second thoracic roots from participation in oculopupillary function.

The lesion may not only implicate the first thoracic root in the Klumpke form of paralysis but the symptoms may indicate that the spinal cord at this level also is affected, and in such an occurrence symptoms of implication of the lower limb on the same side will be obtained. Such a case I have had the opportunity of studying.

E. C., a boy, aged nine years, was referred to me by Dr. C. H. Frazier, October 25, 1917. He had an accident February 17, 1917. While on roller skates he went off the sidewalk, chasing another boy, and ran into a wagon in the street and was thrown against the curb of the sidewalk. When he was found he had a ring about his neck of bruised tissue. The right clavicle was much fractured. The right lower limb was weak about two months and would give away in walking. After this the lower limb gradually recovered normal power. He had never had any pain in the right upper limb except at the setting of the clavicle. He had some pain at first in both lower limbs, lasting about one week. He had never had any loss of sensation in the right upper limb. The right upper lid drooped greatly and the right pupil was much smaller than the left. The right side of the face seemed smaller than the left. He lost two nails on the right hand and the nail of the right big toe after the accident.

In my examination I found the right biceps jerk was prompter than the left. The right triceps jerk was not distinct. He had normal or nearly normal power at the right shoulder and right elbow, but only a little power at the right wrist, no power in the flexor carpi ulnaris muscle and no power in the right fingers. The right arm above the elbow and the right shoulder muscles were not at all atrophied, the right forearm was smaller than the left and the right hand was intensely atrophied. The right palpebral fissure was much smaller than the left and the right pupil was distinctly smaller than the left and the right eyeball was not so prominent as the left. The power in the right lower limb was equal to that of the left. He stood well on either foot alone, but had distinctly positive Babinski, Chaddock and Oppenheim reflexes on the right

side and not on the left side. There was no change in touch, position, heat, cold or pain sensations in either upper or lower limb.

In dorsal flexion of the right hand there was weakness on the ulnar side, probably from lack of tone in the flexor carpi ulnaris muscle.

The case in which oculopupillary symptoms resulted from division of the first thoracic root, to which I have alluded, described very briefly except for these symptoms, was referred to me by Dr. P. H. Swartz, of Towanda, and is as follows:

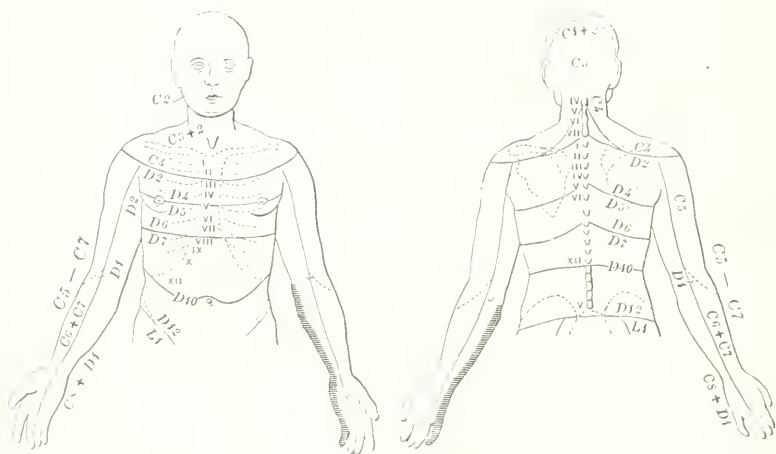
H. B., female, aged eighteen years, had complete paralysis of motion and sensation in the lower limbs and pain radiating in the lower inner side of the left upper limb to the hand, more in the little finger. The left upper limb was a little weak. The thenar and the hypothenar eminence appeared a little flattened in both hands and more distinctly so in the left hand. The fingers of the left hand were held in partial flexion at the second and third phalanges. There were no oculopupillary signs before the operation. The operation was performed by Dr. C. H. Frazier, October 18, 1919.

The spinous process of the seventh cervical vertebra was identified the day previous to the operation by the roentgen rays. With this point approximately as the center of the incision the laminae of the first thoracic and sixth and seventh cervical vertebrae were removed. This exposure, according to the diagram in Dejerine's *Sémiologie des Affections du Système Nerveux*, second edition p. 615, should reveal the seventh and eighth cervical and first and second thoracic segments.

A tumor was found on the left side of the spinal cord in the upper thoracic region and a large posterior root passed nearly across the middle of the tumor. The tumor had much the size and shape of an almond and was cystic. There was marked difference in size between this root and the one immediately below it, as I was able to determine by careful observation, such a difference as is commonly seen between the first thoracic and second thoracic roots. It was necessary to divide this large root near its exit through the dura, as it was involved in the tumor mass, and both the anterior and posterior portions were cut. As far as could be determined by most careful observation the root cut was the first thoracic root and the symptoms resulting justified this conclusion. Following this operation the left palpebral fissure was distinctly smaller than the right and the left pupil was smaller than the right, but both reacted promptly to light and in convergence and the left eyeball was not quite so prominent. During the first few days following the operation sweating was very pronounced on the right side of the face while the left side of the face remained dry, but sweating occurred freely on both sides of the chest, so that the dryness of the left side of the face was the pathological condition. The right side of the face was more flushed than the left.

Following the operation numbness was experienced in the left little finger, the ulnar side of the ring finger, and the ulnar side of the left forearm. This at first was pronounced and was greatest in the little finger, but gradually became less intense, although it did not disappear.

The root that was cut could have been only the eighth cervical or first thoracic, and I believed it to be the first thoracic from its size and relations and the resulting numbness of the ulnar side of the left forearm and hand. The resulting palsy of the sympathetic to the eye was pronounced from the cutting of this one root, and this root evidently contained most of the sympathetic fibers to the eye. The operation was done October 18, 1919, and the palsy of the cervical sympathetic had not changed when the patient left the hospital November 11, 1919.



Showing the area of diminished sensation after division of the first thoracic root. The disturbance was greater in the hand than in the forearm.

She returned December 8, 1919. An examination made December 12 showed that touch, pain, heat and cold sensations were diminished in a narrow band on the ulnar side of the left forearm to within about two or three inches of the elbow and on the ulnar side of the hand, including the little finger. This was only a mild impairment for any form of sensation; a little greater irritation of any of these forms of sensation was promptly and correctly recognized. The impairment was greater in the hand and little finger than in the forearm. The paresthesia had disappeared from the forearm and hand in the area of slightly impaired objective sensation, where it was pronounced immediately after the operation. It persisted in all three segments of the left little finger, but sometimes was felt only in the most distal segment. There was still a

little flattening of the left hypothenar eminence and of the interosseous spaces, but this condition existed before the operation. The thenar eminence was not atrophied. I could not notice any increase of wasting, and the patient believed the left hand was becoming progressively stronger. When the left hand was at rest there was still a tendency to flexion of the fingers at the second and third phalangeal articulations, progressively increasing from the index to the little finger, *i. e.*, the hand had a tendency to assume the position of ulnar palsy. She could fully extend all the segments of the fingers of the left hand without difficulty. The grasp of the left hand was a little weaker than that of the right. Improvement in the lower limbs was very pronounced, and there was possibly a little improvement in the sympathetic supply of the left eye.

Dr. E. A. Shumway reported that when he examined the patient in a position facing the window on a rather cloudy day on December 13, 1919, almost two months after the operation, the right pupil measured 4.5 mm. and the left pupil 3.5 mm. The right palpebral fissure measured 11 mm. and the left 10 mm. in width. No difference in position of the eyeballs could be detected by the exophthalmometer.

Two instillations of a 4 per cent. cocain solution were made in the left eye, with a resulting well-marked dilatation of this pupil, so that there could not have been a complete sympathetic paralysis from division of the first thoracic root, and this would indicate that the first thoracic is not the only root conveying oculopupillary fibers, even though it may convey most of them. Cocain is believed to stimulate the sympathetic fibers to the iris.

I have found a few reported clinical cases believed to be the result of lesion of the first thoracic root without implication of oculopupillary fibers.

In the cases of uniradicular palsy implicating the first thoracic root reported by E. Farquhar Buzzard there was present a partial atrophic palsy of certain muscles of the hand and forearm, and although the amount of atrophy varied slightly in individual instances the same muscles were affected in all. These were the long flexors of the fingers slightly, the interossei muscles considerably and the muscles of the thenar and hypothenar eminences in varying degrees.

He quotes Herringham as maintaining that the first thoracic nerve sometimes supplies in part the flexores profundus and sublimis, the interossei, the hypothenar and deep thenar muscles.

Buzzard admits that the degree of atrophy which obtained in certain of the hand muscles was much greater than might have been expected if only one out of two or more spinal roots had been cut off, and yet he attributes all the changes he found to lesion of the first thoracic root alone. He had no oculopupillary symptoms. He also found marked anesthesia on the ulnar side of the forearm.

These were all purely clinical cases. He quotes a similar case reported by Charcot.

The case reported by Edwin Bramwell is very similar to those reported by Buzzard, and was without operation or necropsy. It was reported as a lesion of the first dorsal root.

Oppenheim in the 1913 edition of his text-book expresses a doubt as to the correctness of the interpretation of these findings, and the findings both of Buzzard and of Bramwell are considerably more extensive than are those obtained by me in the case in which it was definitely known that only the first thoracic root was affected. I believe that in both Buzzard's and Bramwell's cases the lesion must have implicated more than the first thoracic root.

Many of the diagrams of radicular sensory representation are unsatisfactory for the distribution of the eighth cervical and first thoracic roots. Kocher, as represented by Edinger, makes no attempt to separate these two areas, neither does Seiffer. Henry Head and A. W. Campbell, from their study of herpes zoster, give a distribution for the first thoracic root which conforms remarkably closely with the area of disturbed sensation in my patient, except that the area goes in their diagram all the way to the elbow, which is of minor importance. Dejerine's Fig. 365 in her *Sémiologie*, represents a distribution of the first thoracic root which conforms closely to the area disturbed in my patient, but I can find no justification for the representation she gives of this root as a narrow band in the inner side of the arm extending from the elbow to the axilla. Dejerine does not attempt to separate the motor distribution of the eighth cervical and first thoracic roots.

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ON THE EPIDEMIC ACUTE AND SUBACUTE NON-SUPPURATIVE
INFLAMMATIONS OF THE NERVOUS SYSTEM PREVALENT
IN THE UNITED STATES IN 1918-1919: ENCEPHALITIS;
ENCEPHALOMYELITIS; POLYNEURITIS; AND
MENINGO-ENCEPHALO-MYELO-
NEURITIS.¹

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THE CLINICAL PHENOMENA OF THE DISEASE.

This epidemic disease gives rise to clinical phenomena that are referable chiefly to disturbances of the functions of the nervous system. Since any area in the nervous system may be involved, with either loss of, increase of, or perversion of function, and since the single cases vary greatly as to the number and distribution of areas diseased as well as to the intensity of the process in particular areas, we may, in epidemic encephalitis, meet with the greatest variety of neurological syndromes, so that it is not surprising that some clinicians, overlooking an underlying unity, have thought that several of the syndromes correspond to as many different and independent diseases. Just why the intensity of the process and the distribution of the injuries to the nervous tissues are so variable we do not yet know, but there is good reason to believe that in this epidemic we are dealing with a single infectious agent as a cause, and that this agent attacks the central and peripheral cerebrospinal nervous system and its coverings in a widespread, though, at the same time, in a patchy or disseminated way. Under such conditions a great variety of combinations of general and focal symptoms must be expected in a series of cases. An understanding of the underlying pathological-anatomical process in epidemic encephalitis makes clinical diversity no surprise; what arouses wonder is rather the frequency with which certain associations of symptoms, such as lethargy, with fever and ophthalmoplegia, are met with in the epidemic. (See Table I.)

¹ This paper was presented (in abstract) before the Association of American Physicians at its meeting at Atlantic City, in June, 1919, and the abstract will be published in the Transactions of the Association.

TABLE I.—CLINICAL PHENOMENA OBSERVED

Case and date examined, 1919.	N. II. Opticus.	N. III (oculomotorius).				N. IV. Trochlearis.	N. V. Trigeminus.	N. VI. Abducens.	N. VII. Facial.
		Ptoſis.	Ext. bulbar muscles.	Iris.	Accommodation.				
I. C. M. C. Feb. 28	0	Partial bilateral	All weak	Sluggish; anisocoria			Partial paralysis and sensitiveness of rt. masseter; deflection of jaw to rt.	Paresis of right M. rect. lat.	Bilateral facial palsy
II. K. S. C. Feb. 28	0	0	0	Sluggish pupils; anisocoria	Difficulty reading	0	0	0	Bilateral facial palsy
III. N. M. L. Mar. 2	0	0	0	Sluggish; pupils sl. irregular		0	0	0	
IV. K. L. Mar. 13	0	0	0	Miosis and slight irregularity		0	0	0	
V. F. I. Mar. 17		Partial bilateral	Weakness, especially of left M. rect. med.; diplopia	0	Inability to read	0	Sensitiveness of masseters (Thomas's sign).	0	Tremor of lip of six months with lateral palsy of muscles
VI. D. O. H. Mar. 24	0	0	0	Slight anisocoria and sluggish rt. pupil		0	0	0	
VII. F. X. Mar 22	0	Slight right	Diplopia; weakness of all mm. especially superior rect.	Sluggish pupils	Inability to read for week before admission	Bilateral paresis	Bilateral dysmnesia; tender masseters on ninth day.	Bilateral paresis	Bilateral facial palsy
VIII. F. M. T. Apr. 14	0	0	Diplopia	Sluggish pupils	Temporary paresis	0	0	Paresis on left side	

CASES OF EPIDEMIC ENCEPHALITIS.

N. VIII (usticus). chlearis. stibularis.	N. IX. Glosso- pharyngeus.	N. X. Vagus.	N. XI. Accesso- rius.	N. XII. Hypoglos- sus.	Other phenomena.
0	0	Pulse-rate 108	0	0	Undernourished; gastric hyperacidity; 30 small mononuclear cells in c. s. f. with + + + globulin and negative Wassermann.
nitus	0	Pulse-rate 104	0	0	Pain in head and neck; nervousness, emotionalism and weakness; aching pains in legs; insomnia; forgetfulness; irritability; difficulty in walking; mental depression; well-marked Parkinsonian mask; marked drowsiness at onset; rather marked, coarse tremor of head and trunk; finer tremor of fingers; systolic pressure 190, diastolic 120; oral sepsis; slight hyperthyroidism; chronic alcoholism, tabagism and strychninism.
0	0	Pulse-rate 90	0	0	Brudzinski +; Kernig +; Babinski equivocal on left; delirium; history of potatorium; in c. s. f. 133 small mononuclear cells; strongly positive globulin and negative Wassermann; "luetic type" of curve with gold sol. test; alb. and casts in urine with phthalein output of 70; 35 pounds underweight; improvement after lumbar puncture; slight fever.
0	0	Pulse-rate 104	0	0	Reflexes normal; no objective disturbance of sensation, but complaint of persistent numbness and tingling in left arm, left loin and left leg, which came on two days after an attack of influenza, and has progressively increased in intensity; ten days after onset, transitory glycosuria; c. s. f. showed 30 small mononuclear cells, positive globulin and negative Wassermann; moderate obesity and slight arterial hypertension; marked oral sepsis.
0	0	Pulse-rate 112	0	Marked tremor of tongue	Marked Parkinson mask; pronounced apathy and depression; delirium at onset after influenza; c. s. f. showed 7 small mononuclears, positive globulin; negative Wassermann; atypical parietic curve with gold solution test; achylia gastrica; myoma uteri; undernutrition 25 pounds; temperature 99 to 100°.
0	0	0	0	0	Onset with backache, hiccough and girdle pains; later severe root pains in lower extremities and later in chest; slight fever; marked drowsiness for 4 or 5 days; unsteady gait; insomnia; c. s. f. showed increased pressure, 48 small mononuclear cells; globulin + + +; Wassermann negative; improvement after lumbar puncture; fluid a week later showed 14 small mononuclear cells and + + + globulin; positive Oppenheim on right.
0	Slight dys- phagia	Pulse-rate 100	0	0	Slight fever; drowsiness; unilateral sweating of face; lacrymation; headache; mask-like face; c. s. f. bloody but negative Wassermann; slight nystagmus.
0	0	Pulse-rate 84	0	0	Stupor at onset; long standing psychasthenic state; marked oral sepsis; anemia; slight fever; undernutrition.

ONSET. This may be sudden or gradual, and with or without prodromata (asthenia, lassitude, headache, vomiting). Some of the patients regard the attack as influenzal; others give a history of having had influenza a few days or a few weeks before; still others assert that they have not had influenza at all. The general encephalic symptoms may, in some cases, be the more marked at onset; in others, focal symptoms, referable to brain or spinal cord, or signs of meningeal irritation, announce the presence of a nervous disease.

GENERAL SYMPTOMS. The most striking general symptom, when it is present, is a disturbance of the general consciousness that manifests itself in a pathological drowsiness, a symptom that led von Economo to call the disease "encephalitis lethargica," and the lay press to dub it "sleeping sickness." All grades of this disturbance (apathy, dulness, somnolence, sopor, stupor, coma) may be met with, either in a single case or in a series, and either at or near the onset or later in its course. Some patients, however, do not manifest the symptom at all. In one patient of my series, who was drowsy for about a week, the tendency was attributed at first, erroneously, to the effects of codein administered for the relief of pain. Milder involvements of the general consciousness (somnia and sopor), from which the patients can be roused and made to answer questions, seem to have been more common in the epidemic than the severer disturbances (stupor and coma).

Other disturbances of the general consciousness, including mental depression, anxiety and delirium, also frequently occur. A patient may be drowsy in the daytime and complain of insomnia and restlessness at night.

Headache, vertigo, tachycardia and vomiting are common general symptoms. Outspoken choked disk was not present in any of the cases of my series, and, judging from the reports, is not met with, though a slight optic neuritis may occur. Fever may or may not be present at the onset, but is usually evident at some time during the course of the disease. It was slight in most of the cases we have seen, though we were impressed with the persistence of an elevation of temperature of 1° or 2° , extending over a period of from one to three weeks in several of the cases. In some cases there is marked pyrexia, 102° to 105° , lasting for from one to a few days.

FOCAL SYMPTOMS. These are predominantly motor rather than sensory.

Commonest by far are bilateral nuclear and radicular paralyses of the eye muscles (of well-known type), with ptosis and ophthalmoplegia externa et interna (polioencephalitis superior acuta involving N. III, N. IV and N. VI); but pontile and bulbar nuclear and radicular paralyses, with facial paralysis, dysmasesia, dysphagia, dysarthria, etc. (polioencephalitis inferior acuta involving N. V (motor), N. VII, N. IX, etc.), are also common, as are symptoms pointing to paralysis of part of the extrapyramidal motor system

(Parkinsonian mask; loss of the normal facial innervations accompanying the emotions). The lesions that are most frequent as causes of motor focal symptoms in epidemic encephalitis must therefore be located in (1) the midbrain about the aqueductus cerebri, (2) the pons and upper medulla oblongata and (3) the basal ganglia (globus pallidus?).

Less common motor disturbances in epidemic encephalitis, though they may occasionally be encountered, are monoplegias, hemiplegias, diplegias, aphasias, contractures, choreatic and athetotic disturbances of motility and general or circumscribed convulsive seizures.

Focal phenomena of a sensory nature are much less frequent than those of a motor nature above referred to. Nevertheless, sensory symptoms due to focal lesions of the sensory areas (cortex) and paths (corona radiata; lemnisci) are occasionally met with (hemi- or mono-anesthesias; paresthesias; hyperesthesias; algias; more rarely, hemianopsia). In one of our cases, in which there was a meningomyelo-encephalitis, severe root-pains in the trunk and lower extremities were prominent.

Acute ataxias of different types (according to the localization of the lesions) may be exhibited. The commonest form is the cerebellar type, due doubtless to lesions of the cerebellum or its peduncles or of the red nucleus mechanisms.

MENINGEAL SYMPTOMS. Only in relatively few cases are the clinical signs of an outspoken meningeal irritation present. In one case of our series there was pain in the neck and back, some rigidity of the neck, a positive Brudzinski sign and a positive Kernig sign. von Economo, S. A. K. Wilson and others have reported similar cases. That there is a slight patchy involvement of the leptomeninges in the inflammatory process in many cases has been shown, however, by postmortem examinations and by the increased cell count and the positive globulin reaction in the cerebrospinal fluid.

CEREBROSPINAL FLUID. This may or may not be under increased pressure. The fluid looks perfectly clear, and no film, as a rule, forms on standing. In some undoubted cases of the disease the cell count has been normal and the globulin test negative. The apparent normality of the fluid on naked-eye examination apparently misled many of the European observers, who made the earlier reports on the disease, to declare that no changes are present in the cerebrospinal fluid. Abnormal fluids have been very constantly encountered in our own cases, though they would have been overlooked because of the apparently normal macroscopic appearances had the examiner failed to make a cell-count and a globulin test. *In our experience, a cell-count in the cerebrospinal fluid of from 10 to 100 small mononuclears along with a positive globulin reaction with negative Wassermann and negative bacteriological smears and cultures*

is, at the time of an epidemic of encephalitis, strong corroborative evidence of the existence of the disease in a patient in whom the process is for any other reason suspected to exist. (See Table II.)

TABLE II.—CEREBROSPINAL FLUIDS IN EPIDEMIC ENCEPHALITIS.

Case.	Day of disease.	Appearance.	Pressure.	Globulin.	Number and variety of cells.	Wassermann reaction.
I. C. M. C.	19th	Clear, colorless	++++	30	0
II. K. S. C.	106th	Clear, colorless	Increased	++++	11	0
III. N. M. L.	21st	Clear (fairly)	Increased	++++	97	0
	23d	?	?	?	Increased; 98% lymph., 2% leuko.	?
IV. K. L.	26th	?	?	+++++	133	0
	75th	Clear	Increased	+	33	0
	66th	?	Normal	+	30; lymphocytes predom.	0
V. F. I.	51st	25 c.c. cl. fluid	Not increased	+	2; lymphocytes	0
	53d	?	?	Weak; pos.	?	0
	66th	?	?	++	7	0
VI. D. O. H.	29th	Clear, colorless	Much increased	+++	48; sm. monos.	0
	36th	Clear, colorless	Much increased	++++	14; sm. monos.	0
	41st	Clear, colorless	Increased, but not so much as formerly	++++	14	0
VII. F. X.	7th	Bloody	?	?	Bloody?	0
	13th	Bloody	Not increased	?	?	?

Negative findings in the cerebrospinal fluid do not, however, rule out the disease.

Still another point regarding the cerebrospinal fluid is worthy of comment. In more instances than accidental injury to a small bloodvessel will apparently account for, a bloody fluid is obtained on lumbar puncture in patients suspected to be suffering from the disease. This point has been noted also by other observers, and it seems likely that the well-known hemorrhagic tendency in the disease is thus sometimes manifested.

TABLE III.—BLOOD IN EPIDEMIC ENCEPHALITIS.

Case.	Day of disease.	Red blood cells.	Hemoglobin, per cent.	White blood cells.	Polymorphonuclear neutrophils, per cent.	Polymorphonuclear eosinophiles, per cent.	Polymorphonuclear basophiles, per cent.	Small mononuclears, per cent.	Large mononuclears and transitionals, per cent.	Wassermann.
I. C. M. C.	21st	5,212,000	90	6,200	62.0	2.0	0.4	23.2	12.4	0
II. K. S. C.	105th	5,536,000	95	12,800	87.2	0	0	9.6	3.2	0
III. N. M. L.	19th	4,844,800	90	22,850	90.0	1.0	1.0	7.0	1.0	0
IV. K. L.	60th	5,472,000	90	10,000	76.0	0.4	0.0	17.2	6.4	0
	42d	5,856,000	85	10,000	82.8	0.0	0.0	12.8	4.4	0
V. F. I.	57th	?	90	7,700	?	?	?	?	?	?
	30th	4,800,000	85-90	9,000	?	?	?	?	?	0
VI. D. O. H.	7th	6,328,000	77	9,120	75.5	1.0	0.0	16.0	7.5	0
	9th	6,512,000	75	9,820	76.0	1.0	1.0	13.0	9.0	0
VII. F. X.	19th	5,280,000	78	7,800	75.0	0.7	0.0	18.7	5.7	0
	30th	5,408,000	97	17,600	70.4	0.4	0.4	22.8	6.0	0
	62d	3,600,000	70	3,058	72.4	1.2	0.0	18.0	8.4	0

THE BLOOD. A slight leukocytosis is usually present. The white cell count in our cases varied between 3058 and 17,600. per c.mm., except in one instance in which the cell count was 22,850. The differential count of the white cells usually, though not always, reveals a slight relative and absolute increase in the polymorpho-nuclear neutrophile elements (70 to 90 per cent. of the total white count). (See Table III.)

THE URINE. A trace of albumin and a few casts are sometimes demonstrable, doubtless due to a slight toxic degenerative nephropathy such as is met with in most acute infectious processes. Renal function, as far as the pthalein test has been applied, appears to be unimpaired. When severer renal disease, as in chronic alcoholism, accidentally accompanies encephalitis with lethargy, the differential diagnosis may be difficult as in one case of our series in which the delirium and coma were thought, at first, to be due to uremic intoxication.

DURATION OF THE DISEASE. Whether the disease terminate in death or in recovery, the course may be either brief or prolonged. In severe fulminant cases death may occur in a few hours or days. In many instances, both mild and severe, recovery has been rapid, the symptoms lasting from a few days to a month. In the majority of cases, however, the disease is a protracted one, extending over many weeks, and in some instances over several months.

PROGNOSIS. As regards life this is much better than might have been expected, even in cases that at onset present the gravest symptoms. The mortality has been variable in different countries, and seems to have been greatest in Austria and in France. Six out of 11 of the cases reported from Austria by von Economo died; 7 of Netter's 15 cases reported from France were fatal; only 2 of S. A. K. Wilson's 13 cases reported from London were fatal; in our own series it happens that there have been no deaths at all, due to accidental encounter of a mild group of infections. Though just what the mortality rate has been in the United States it is as yet difficult to estimate. Bassoe, Pothier, and Tucker have all reported fatal cases, and the newspapers have given evidence of many deaths all over the country from "sleeping sickness."

As regards residues and sequelæ in the patients who recover, it is, as yet, of course, too early to make any definite statement. We have been impressed, on the one hand, with the very remarkable improvement observable in some instances within a few weeks (disappearance of paralysis; recovery of facial expression and vanishing of the Parkinsonian mask; replacement of depression by normal mood), and, on the other hand, with the persistence in some cases over a long period of the eye-muscle disturbances, the dizziness, the depression and the asthenia.

We must be on the lookout in the coming period, we believe, for sequelæ, especially, as it would seem likely that large numbers of the

milder infections must have gone entirely unrecognized. We have the fear, let us hope that it is not well-founded, that, as a result of the epidemic, we may see an increased incidence, later on, in the conditions hitherto known as "multiple sclerosis," unexplained "mental deterioration," and "idiopathic epilepsy."

NATURE OF THE DISEASE.

Observers had but little difficulty in determining early in this epidemic that they had to deal with an infectious, or toxi-infectious, process involving predominantly the cerebrospinal nervous system. The clinical phenomena of an epidemic disease (of acute onset with fever) that manifested itself by a disturbance of the general consciousness and by paralyses, especially in the domain of the upper, and sometimes of the lower, cerebral nerves left no doubt on this point; but had there been any doubt it would soon have been dissipated by the necropsy findings, which revealed lesions of an inflammatory, and sometimes of a hemorrhagic, character disseminated throughout the nervous system and its coverings (encephalitis; encephalomyelitis; meningo-encephalomyeloneuritis). The resemblance of the clinical features in single cases to various well-known and less well-known syndromes (Wernicke's "polioencephalitis superior acuta;" Strümpell's "primary acute encephalitis;" Wickman's "encephalitic form of the Heine-Medin disease;" Leichtenstern's "post-influenzal encephalitis;" "acute infectious polyneuritis;" botulism with ophthalmoplegia; the mysterious epidemic disease known as "nona" in 1890; and the epidemic "sleeping sickness" (*Schlafkrankheit*) described after a grippe epidemic in Tübingen by Camerarius as far back as 1718) was quickly detected by one or another of those who had opportunity to study the outbreak. An epidemic of an acute infectious (and inflammatory) disseminated meningo-encephalomyeloneuropathy closely resembling, if not identical with, certain diseases earlier described had, then, presented itself in many different countries of the world for study and for consideration.

Concerning the etiology of the disease, very different opinions have been advanced. Some investigators, especially those who studied in the first two or three areas of what is now seen to be a pandemic distribution of the disease evidently thought that they were dealing with an entirely new malady. Thus, von Economo, who, in Austria, described it as "encephalitis lethargica," Bradford, Bashford and Wilson, who studied a special group of cases in the British Expeditionary Force and designated it "acute infectious polyneuritis," and Netter, who in Paris described it as "encéphalite léthargique épidémique," all seem inclined to regard it as a new disease, though they admit its resemblance to recognized diseases. It was soon seen, however, on analysis of the clinical phenomena

and the pathological-histological findings, that under some one or other form of encephalitis, or of encephalomyelitis, parallel phenomena have already been described in medical literature. Thus most of the phenomena, both clinical and histological, will be found paralleled in the larger collective reviews of acute non-suppurative encephalitis, such as those by Chartier (1907), by Oppenheim and Cassirer (1907) and by Vogt (1912). Most of the cerebral-nerve paralyses will be found duplicated in the cases of encephalitis tabulated by Wilbrand and Saenger (1900). Most, if not all, of the pathological-histological findings appear to be in accord with those described by Friedmann (1890-1898), Bücklers (1892), Flatau (1900), Spielmeier (1902) and Raymond and Cestan (1904). One of the English writers (S. A. K. Wilson) concludes that "what appears to be new is the occurrence in epidemic form of cases of encephalitis not to all appearance due to the action of a known infective or toxi-infective agent, but presenting clinical symptoms any or all of which have been noted in various kinds of encephalitis with which the neurologist has long been conversant." But is even the occurrence in epidemic form new? Have we not records of one epidemic by Camerarius in 1718, of another by Lepecq de la Clôture in 1763, of at least three mentioned by Ozanann (in his history of epidemic diseases) as occurring in 1745, in 1800 and in 1802, of an epidemic of encephalitis described by Leichtenstern after the great influenza epidemic of 1889-1890, as well as of epidemics of "nona" that occurred at about the same time (reports collected and reviewed by Longuet in 1892)? In England the first cases observed in the present epidemic of encephalitis were thought to be instances of meat-poisoning (botulism). The problem of etiology as at present discussed for the recent epidemic resolves itself into three questions: (1) Is the disease due to the virus that causes influenza? (2) Is the disease due to the virus that causes the Heine-Medin disease or to a modification of that virus? and (3) Is the disease due to a virus *sui generis*?

The possibility that the virus that causes influenza may also be the cause of the encephalitis recently pandemic is well worthy of serious consideration; for we have good reason to believe that encephalitis, like meningitis, like pleuritis, like nephritis and like other inflammations, may at different times be due to entirely different causative agents. Thus it is well-known that non-suppurative encephalitis may occur as a complication of scarlet fever, of measles, of chicken-pox, of whooping-cough, of pneumonia, of anthrax, of malaria, of poliomyelitis and of other infectious diseases, and it is probable that these complicating inflammations of the brain are due to local infection of the nervous system with the specific virus that causes the primary general disease rather than that they are all instances of mixed infections of a unitary virus causing encephalitis and of the specific viruses of the several

infectious diseases mentioned. Now if this view be a correct one it is surely not a wholly improbable supposition to suggest that an epidemic, or a pandemic, of encephalitis occurring in association with or soon after an epidemic, or a pandemic, of influenza may be due to an encephalic localization of the influenzal virus. Indeed, the encephalitis that was described by Leichtenstern, in 1890, is generally referred to in the literature as "influenzal encephalitis," and it may be recalled that Pfühl, and later Nauwerck in fresher material, asserted that they had demonstrated the presence of the *Bacillus influenzae* of Pfeiffer in the diseased cerebral tissues in "influenzal encephalitis." Though the latter demonstration is at present less convincing than formerly, owing to the reopening of the question of the etiology of influenza itself and to the doubt cast upon Pfeiffer's bacillus as its cause,¹ still the occurrence of encephalitis in epidemic (and in pandemic) distribution in such close connection with epidemic (and pandemic) influenza as that observed in 1890-1892, and as that at the present time, strongly suggests at least one of the three following possibilities: (1) that the influenzal virus is the cause of the epidemic encephalitis, (2) that influenzal infection predisposes to infection with the virus of encephalitis, or (3) that the cosmic influences that determine the occurrence of epidemic influenza also determine the occurrence of epidemic encephalitis, even if each disease is due to a separate and distinct virus. It may be argued also that influenzal encephalitis tends to assume a special clinical form (acute cerebritis), but certainly other forms also occur in the epidemic; indeed, in the present outbreak, the polioencephalitis-superior type has predominated. Granting the weight of the arguments adduced, it must be admitted, however, (1) that the incidence of epidemic encephalitis is very low compared with that of influenza, (2) that the available data do not permit of the assertion of any direct parallelism of incidence and distribution in the two diseases, and (3) that some of the patients who have suffered from encephalitis deny any preceding attack of influenza, though doubtless all have been exposed to that disease. Thus until we are sure of the precise nature of the virus of influenza on the one hand and of the virus of epidemic encephalitis on the other, the questions regarding the exact etiological relationships of the two diseases must be left open.

It is but little wonder, too, that some have thought that the virus of epidemic encephalitis may be identical with, or a slight modification of, the virus (*Flexneria noguchii*) that is the cause of the Heine-Medin disease (poliomyelitis anterior acuta). For, in the first place, since Wickman's studies, cerebral, pontile, cerebellar, bulbar and meningeal forms of the Heine-Medin disease are certainly known to occur. And, in the second place, the pathological-histological lesions in the central nervous system and the findings in the cerebro-

¹ Cf. Bloomfield, A., and Harrop, G., et al.

spinal fluid in epidemic encephalitis and in poliomyelitis show a close resemblance. But against the view of identity there are many facts that may be urged. The onset of the paralysis is very different in the two diseases, since in poliomyelitis the paralysis is all there from the beginning, whereas in epidemic encephalitis the paralysis begins insidiously, often as ptosis or loss of power of accommodation, and gradually extend through a period of several days or longer to other muscles. Bilateral symmetry of the paralysis is more common in encephalitis, unilateral or asymmetrical paralysis in the Heine-Medin disease. The fever is usually slight and often more marked after the paralysis has developed in encephalitis; in the Heine-Medin disease the fever is, as a rule, highest before paralysis occurs. There is a much higher leukocytosis in the blood and also a higher cell count in the cerebrospinal fluid in the Heine-Medin disease than in encephalitis. The age-incidence is also different, since encephalitis is common at all ages of life, whereas the Heine-Medin disease shows a special predilection for childhood and adolescence. Again, a careful study of the distribution of the cases of encephalitis and of poliomyelitis in England has shown that the two series of cases are distributed independently of one another. And, finally, if there were identity of etiology one would expect more typical encephalitis cases in epidemics of poliomyelitis and more typical poliomyelitis cases in epidemics of encephalitis than we actually see. Some investigators, though fully granting that there may not be identity of etiology, suggest that the virus of encephalitis may be one special strain and the virus of poliomyelitis another special strain of a single microorganism, just as we now recognize Type I, Type II, and Type III, etc., of the *Pneumococcus*, or recognize that *Bacillus paratyphosus A* and *Bacillus paratyphosus B* are two strains producing similar but not identical diseases. In favor of this view may be adduced the findings of von Wiesener, of Vienna, who asserts that he has isolated an organism (globoid diplococcal form) from encephalitis and reproduced the disease in monkeys, and that this virus resembles closely that isolated by Flexner and Noguchi in poliomyelitis. A similar virus seems to have been grown by Wilson from Bradford's "acute infectious polyneuritis" cases, and with this virus it was also possible to reproduce in monkeys what they believed to be the disease they had under study. Cleland and Campbell assert that they have successfully conveyed the virus of the disease to the sheep, the calf and the horse. It is, of course, possible that just as we have a group of diseases (the leishmaniasis) due to different strains of species of *Leishmania*, so we may have a group of diseases (the flexneriasis) due to different strains or species of an organism (*Flexneria*), of which the virus of the Heine-Medin disease is one. But until more extensive virus studies and experiments have been made it would be unwise to look upon such a view as anything more than an interesting speculation.

That epidemic encephalitis may, finally, be due to some causative agent neither identical with nor even a modification of any other virus is quite possible, and is, indeed, the view held by a number of those who have studied the disease. If this view turn out to be the correct one it will be interesting, later on, to find out whether the virus isolated by von Wiesener, that isolated by Wilson, or some entirely different filtrable (or unfiltrable) virus is the etiological agent.

TREATMENT OF EPIDEMIC ENCEPHALITIS.

The patients under our observation have evidently been of the milder type, as none of them died. Convalescence has been tedious in several of them, and in how far there will be residual phenomena in some, it is as yet too early to be sure.

At the onset of the disease, rest in bed, protection from external stimuli of all kinds, laxatives, bland diet and relief of headache and of pains would seem to be desirable.

In our experience, lumbar puncture, done for diagnostic reasons, relieved the symptoms so markedly in several instances that it was repeated at intervals as a therapeutic measure.

During convalescence, prolonged rest, careful nursing, a nutritious diet and mild hydrotherapy, electrotherapy and massage have been the only measures made use of. Complete recovery without residuals seems to be common.

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**PLEURAL EFFUSION WITH INVERSION OF THE DIAPHRAGM
PRODUCING AN ABDOMINAL TUMOR; TOGETHER
WITH REMARKS ON ACUTE PULMONARY
EDEMA FOLLOWING TAPPING.¹**

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A NUMBER of years ago I made an autopsy at the Philadelphia General Hospital on a case of left-sided pleural effusion. On opening the abdomen I found in the left upper quadrant a large, smooth, tense tumor which upon further exploration proved to be a bag made by the inverted diaphragm and filled with pleural fluid. The incident made a deep impression upon me, but was not duplicated in my further experience as pathologist. I have, however, seen this tumor twice since then, clinically. Of the first case I cannot find any record; the second I saw a few months ago; it is as follows: The patient is a widow, aged seventy-seven years, who came under my observation in April, 1918. The salient points in her case are as follows: For years she has suffered with diabetes mellitus and chronic nephritis with moderate hypertension. She has diabetic cataract and retinal hemorrhages. When I first saw her, the heart was slightly enlarged; there was a soft systolic mitral murmur; the legs were somewhat edematous. The urine contained sugar up to 3.2 per cent.; and albumin from traces to 2.8 grams per liter. Ketones were inconstantly present. The quantity of urine

¹ Read before the Section on Medicine of the College of Physicians of Philadelphia, October 27, 1919.

was usually about 1500 c.c.; specific gravity varied from 1007 to 1013. Unlike most cases in which nephritis and diabetes coexist, the sugar in this patient did not vary in inverse proportion to the albumin—the larger amounts of sugar were often found when the albumin content of the urine was high.

Under treatment the patient improved greatly and was able to spend the summer of 1918 very comfortably in Atlantic City. On July 25, 1919, I saw her at her home in Wilkes-Barre with Dr. Bullard. It appeared that after eating some cheese on June 5, she had been seized with an attack of acute indigestion characterized by abdominal pain radiating to the back, nausea, vomiting, and slight diarrhea. Within a few days thereafter she began to suffer from shortness of breath and fluttering of the heart which kept her confined to her room. I found her sitting up, intensely short of breath; the lips somewhat cyanosed; pulse rapid; no fever. Making a cursory examination of the abdomen I detected on the left side a large, tense, rounded mass, slightly uneven, somewhat tender, and



occupying nearly the entire upper left half of the abdominal cavity. It extended forward to the prolonged midclavicular line and downward to the level of the umbilicus (see figure). I was at first somewhat nonplussed by it, but found the explanation when I examined the chest. The left chest was visibly distended and enlarged. The percussion note was flat from above the left clavicle down to the bottom of the thorax, front and back. No heart sounds could be heard on the left side; the apex beat was distinct both on palpation and on auscultation in the fifth interspace just within the right nipple line. Over the left chest bronchial breathing and a twangy bronchophony could be heard. I concluded that the abdominal tumor was the inverted diaphragm containing pleural fluid, a view confirmed by the results of tapping the chest.

After drawing off the fluid, which was done slowly, five pints being obtained, the tumor could no longer be felt. Fearing the possibility of pulmonary edema on account of the presumably long duration of the effusion, I remained for a considerable time at the

patient's bedside. In the first half hour nothing happened; the patient was comfortable and greatly relieved of her shortness of breath. Then suddenly the lungs filled up with fluid, loud bubbling rales could be heard everywhere throughout the chest; the breathing became rattling and terribly labored. A violent cough which brought up only a little fluid added to the distress of the patient whose air hunger was painful to see. Her face became purple; the skin cold and clammy; dissolution seemed imminent. I gave her a hypodermic injection of morphin and atropin, which in other cases of this type I had seen productive of good results, but it had no effect. I then applied a number of dry cups over the back, and as if by magic every rale disappeared. I have never seen anything quite so dramatic. The grandson who was present in the room and who had been a most anxious spectator was amazed beyond expression by the instantaneous improvement.

After a proper interval I removed the cups; there was an immediate return of edema, but it was slight and caused little distress. From that time on the patient's improvement was rapid, and she was able to go to Atlantic City the latter part of July, where I had the pleasure of seeing her with Dr. William W. Fox. A considerable accumulation of fluid had again taken place and the abdominal tumor had reappeared, but was not as large as before. Sometime later Dr. Fox tapped the chest, the tumor vanished, and the patient was relieved of her distress. As I know from frequent reports she is in good condition to this day.

I have looked through many text-books on diseases of the lungs and through recent and old works on physical diagnosis without finding more than two references to the diaphragmatic inversion.

Wilson Fox in his monumental work,² mentions it in the following words: "When the effusion is large, the diaphragm may pass below the ribs and may there, in some cases, be felt as a tumor."

Collet³ describes the condition clearly, although he does not bring out the fact that a real tumor-like mass may appear in the left upper abdomen. He says: "Dans les épanchements énormes qui écrasent le diaphragme au point de le faire bomber dans l'abdomen, la matité franchit les limites de l'aire de Traube et dépasse de plusieurs travers de doigt le rebord costal."

The condition is a mechanical result of great intrapleural pressure. As pointed out by Powell and Hartley⁴ "the negative pressure within the pleura is maintained until the lung is completely retracted before the advancing fluid; thereafter any further accumulation compresses the lung and by its weight and pressure forces down the diaphragm." To invert the diaphragm, however, to turn it inside out, a much greater pressure than ordinarily exists in pleural

² Diseases of the Lungs and Pleura, London, 1891, p. 983.

³ Précis des mal. de l'appareil respir., Paris, 1914, p. 501.

⁴ Diseases of the Lungs, London, 1911, p. 97.

effusions must be produced. If the patient is up and about, gravity probably acts as a favoring factor.

It is evident that a tumor formed by a bag of pleural fluid projecting into the abdomen must be considered in the differential diagnosis of abdominal masses. If the chest condition is overlooked, or when not overlooked, if the pleural effusion and the abdominal tumor are not correlated, the possible diagnostic errors are many. The tumor has a peculiar bulky feel, is tender to touch, does not move with respiration, has the shape neither of the spleen nor of the kidney, and appears to have a deep attachment. Its true nature is revealed after aspiration of the chest, when it will be found to disappear. In the absence of tapping a roentgenologic examination is probably the best means of diagnosing the true nature of the tumor. Such an examination will likewise show whether after tapping the diaphragm has returned to its normal position and is functioning properly.

Several years ago in a paper on "Albuminous Expectoration Following Thoracocentesis,"⁵ I referred to acute pulmonary edema following tapping, ascribing it to "congestion by recoil." It is very alarming and sometimes terminates fatally. Usually a hypodermic injection of morphin and atropin brings speedy relief, but, as in the case just cited, it may fail. The remarkable results produced by dry cupping, which cannot be questioned, must be due to some reflex nervous influence. I believe dry cupping to be a good therapeutic measure in all forms of acute pulmonary edema whether due to tapping or to other causes.

RETROPERITONEAL LIPOSARCOMA: REPORT OF AN UNUSUALLY LARGE SPECIMEN, WITH CHEMICAL ANALYSIS.

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SOME time ago one of us made an investigation of the reputed ability of lipomas to retain or even to lay on fat when the body of the host is losing fat, perhaps to the extent of extreme emaciation.¹ The positive evidence recorded in the literature was found to be very scanty, and there were instances in which the lipomas had decreased in size when the host was losing weight. Analyses of lipoma fat have not shown any detectable difference from the fat

⁵ AM. JOUR. MED. SC., April, 1902.

¹ Wells: The Fat Metabolism of Lipomas, Arch. Int. Med., 1912, x, 297.

of normal fatty tissues to explain why it cannot be utilized for the nutrition of the body, and experiments with the fat-splitting enzymes of lipomas did not indicate any significant difference from the enzymes of fatty areolar tissue that could be detected by the crude methods available. The literature does establish, however, that malignant fatty tumors continue to grow while the host is becoming emaciated.² This is especially true of the malignant retroperitoneal fatty tumors, which are so often of very great size, constituting, as a class, probably the largest of the solid tumors.

These retroperitoneal tumors of fibrous and fatty tissue, developing slowly and recurring occasionally after removal, are reported fairly often in the literature, some of them having attained large dimensions. Their peculiar interest seems to rest largely with this slow expansile growth and the unusual size that some have attained. Because of their structure these tumors have received various designations, such as myxoma lipomatodes, lipoma myxomatodes, lipoma edematosum myxomatodes, myxoma undergoing fatty degeneration, myxolipoma, myxo-fibro-lipoma, myxo-sarco-lipoma, etc. Without doubt the tumors described under these various designations could be grouped under one general name, for each contains fibrous and fatty tissues in different proportions, usually with more or less malignant degeneration. Robertson,³ in his review of the literature, records the frequency of these retroperitoneal tumors, gives the gross and the microscopic characters, and includes other special features, such as the weight where this has been mentioned. He collected 51 recorded cases of tumors of this histological type, adding one of his own. Of these, 17 were retroperitoneal and 3 in the mesentery, most of the others arising in the arm or leg.

Gardner and Adami,⁴ in 1900, reporting the occurrence of tumors of this kind, stated that Waldeyer up to that time had recorded the largest. This neoplasm weighed sixty-three pounds, had developed in the mesentery and had formed secondary metastases in the liver and lungs. McConnell⁵ in 1908 described a tumor arising in the right kidney region, which he considered a hypernephroma that had undergone fatty changes accompanied by a limited tendency toward malignancy. The description given is, however, not adequate to decide the point of origin of the growth, and its general features suggest its origin in the perirenal fatty tissues. The entire tumor removed surgically weighed sixty-five pounds, and at a subsequent operation, six and a half years later, a recurrent growth

² Adami: Montreal Med. Jour., 1897, xxv, 529. Voekler: Deut. Ztschr. f. Chir., 1908, xcix, 149.

³ Lipoma Myxomatodes, Jour. Med. Res., 1916, xxxv, 130-146.

⁴ On a Case of Retroperitoneal Lipoma (Lipoma Myxomatodes) with Accompanying Retroperitoneal Fibroma (Chondromyxofibroma), Montreal Med. Jour., 1900, xxix, 417-421.

⁵ Recurrent Liposarcoma of the Kidneys, Jour. Med. Res., 1908, xix, 225.

weighing twenty-seven pounds was removed. McConnell's tumor to date is the largest of its kind recorded in the literature.

We have had the opportunity to study a typical example of a fatty retroperitoneal tumor of the classical type, which happens to exceed in size the largest tumors previously reported and which illustrates exceedingly well the parasitic capacity of tumor tissue to hold fat needed by a greatly emaciated host. In addition a chemical analysis of the tissue has been made which throws some light on the character of the tumor.

CASE HISTORY.—The bearer of this tumor was a white male, aged fifty-five years at the time of his death in the Cook County Hospital, March 1, 1917. The clinical history is briefly as follows:

The patient entered the hospital the first time April 4, 1915, and complained of shortness of breath, with moderate cough, swelling of abdomen and feet, loss of appetite and weakness. He stated that the trouble started eighteen months before. At that time he noticed a swelling of the abdomen and later the feet also became swollen. Swelling of the feet and shortness of breath have recurred several times since, the last attack occurring ten days before entering the hospital. These last attacks were much more severe and were accompanied by slight pains in the left iliac fossa. Swelling of the abdomen has been gradual. Appetite has been poor for several weeks. He has had no gastric pain, but occasionally has a sense of fulness, which is sometimes accompanied by vomiting after coughing spells. This condition has no relation to meals or to food eaten. He has had difficulty in starting urine, and dribbling occurs at the end of urination. He had had no previous illness until two years ago, when he was operated on for inguinal hernia, and a tumor was removed in the lower part of the abdomen. He had gonorrhoea and chancre twenty-six years ago. He drinks two or three whiskies a day. Even at that time, two years before his death, emaciation was very marked. The blood count was 5,100,000 reds and 10,300 whites.

On examination the abdomen showed marked distention and the veins on the lateral wall of the abdomen were greatly distended. Nodular masses were present in the abdomen, especially in the epigastrium. Dulness was distributed irregularly over the entire abdomen. There was dulness in the flanks and an umbilical hernia was present. Paracentesis yielded no fluid on the first attempt, but a second trial gave 5 c.c. of fluid, which contained large lymphoid cells and many eosinophiles showing peculiar mitotic figures. A Wassermann test of the blood was negative. A diagnosis of carcinomatosis of the peritoneum was made and the patient left the hospital April 12, 1915.

He returned to the hospital September 8, 1915, with the same complaints as before. Previous history was verified and examination showed practically the same condition as before. He had gained

nineteen pounds, but the face and neck were still greatly emaciated. He had passed bright red blood from the rectum lately, but had no pain on defecation. Upon lying down he did not show the dyspnea which a cardiac case with the same amount of dyspnea would show. The heart and lungs were both compressed. The liver was large and hard. Hemorrhoids were present. A large amount of ascites was described, but on paracentesis only 40 to 50 c.c. of clear pale yellow fluid was obtained. A diagnosis of inoperable carcinoma of the peritoneum was made and the patient was discharged September 18, 1915.



FIG. 1.—Photograph of patient a few days before death, showing distention of abdomen produced by retroperitoneal tumor.

He reëntered the hospital February 23, 1917, and his appearance at this time is shown by the photographs. In addition to his former complaints he stated that he had difficulty in urination and defecation. He urinates every twenty minutes, and very small amounts each time. He now drinks five or six whiskies a day. Paracentesis

yielded 50 c.c. fluid, which was slightly blood-tinged. The Wassermann test was negative. The blood showed 12,800 leukocytes. Urine contained fine granular and coarse granular hyaline casts, a few red blood cells and a few epithelial cells. The fact that the patient had lived nearly two years after the first diagnosis of inoperable carcinoma of the peritoneum was made rendered this diagnosis most improbable, and it was thought that there must be a cystic condition, presumably loculated, because of the small quantities of fluid obtained by puncture. Therefore, laparotomy was performed by Dr. Kellogg Speed February 27, 1917.

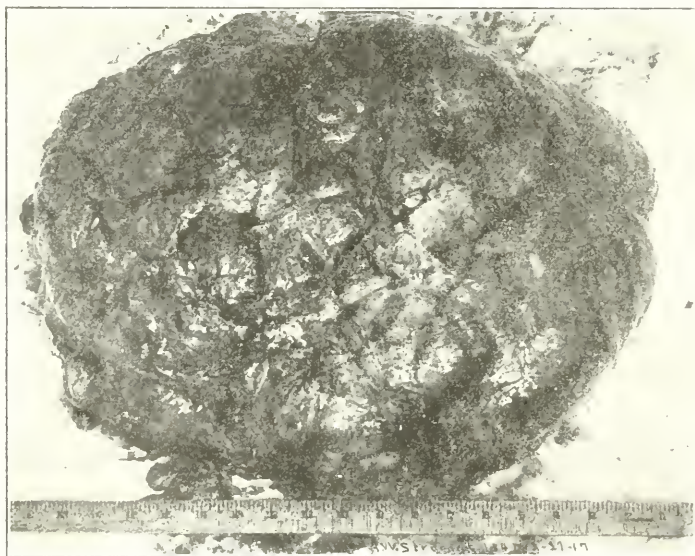


FIG. 2.—Tumor mass removed at operation.

A large tumor mass was found between the anterior two layers of the mesentery. It was approximately the size of five adult heads, and the surface was smooth, irregular, glistening and of medium consistency. Fig. 2 shows the gross appearance of the tumor mass removed at operation. It was bound to the mesentery by tough adhesions. A large kidney-shaped mass could be seen on the right side, and between the posterior two layers of mesentery two other tumor masses could be palpated. One was firmly bound down by adhesions and seemed to be attached to the spleen, which was also enlarged. The liver was easily palpated, but was exceedingly small and shrunken. The stomach could not be located. Most of the intestines were found in the lower quadrant of the abdomen. In one part of the transverse colon a small puncture wound was caused by tearing off an adhesion. The tumor mass between the anterior two layers of mesentery was removed and the wound closed. This

mass, which weighed 14,340 grams, is described in the autopsy protocol. The remaining portion of the tumor could not be removed. Following the operation the patient remained in a collapsed condition and died after about forty-eight hours, on March 1.

The appearance of the patient a few days before the operation is well shown in the accompanying photograph.

AUTOPSY FINDINGS. The autopsy was performed a few hours after death and the significant features are given below.

External Appearance. The body is that of an extremely emaciated man, 162 cm. tall. The legs are slightly edematous, the left more than the right, and the abdomen is greatly distended. The face, arms and chest are greatly emaciated. The umbilicus is very prominent, and a huge recent incision, 30 cm. in length, extends along the midline of the abdomen, closed with catgut and skin clips. A large mass can be palpated in either flank. The external genitals are very edematous. There is a nodular mass, 9 cm. by 6 cm., in the right inguinal canal, and there is the scar of an operative wound over the right inguinal canal. The scrotum is stretched. There are superficial ulcers on the right leg. The veins of the left leg are distended. There is a sutured incision in the bend of the right elbow. The present circumference of the abdomen is 100 cm.

Abdominal Cavity. There is extremely little subcutaneous fat. The subcutaneous tissues in the abdominal wall are edematous and hemorrhagic. The fibrous tissue in the midline is distinctly hypertrophied. There is about a liter of fluid, somewhat blood-stained, in the peritoneal cavity. A tumor, recently removed by surgical operation from the abdominal cavity, was also examined. It is nodular, with adhesions of highly edematous connective tissue, very soft, jelly-like, pale and semisolid. The cut surface is gelatinous and watery, divided into lobules 5 to 10 cm. in diameter, but no definite cyst formation is present. This tumor mass weighs 14,340 grams.

A sutured incision in the peritoneum, about 15 cm. long, indicates the site of the pedicle of the removed tumor mass, at the root of the mesentery, where it grew forward from the mass of similar retroperitoneal tumor tissue.

The abdomen is still filled with the same kind of tumor tissue, covered with peritoneum. It arises in the root of the mesentery and is smooth and movable, and there is no inflammation of the peritoneum.

There are fresh adhesions along the point where the tumor was removed. The upper portion of the tumor is softer than the lower portion. A portion of the tumor mass extends under each psoas muscle; these masses each measure about 7 x 4 x 5 cm. A tumor mass continuous with the large mass extends down into the right inguinal canal. This entire tumor mass is very similar in structure and composition to the one that had been removed. It measured,

on removal, 45 x 20 x 15 cm., and weighed 17,300 grams. One small area of this tumor is pinkish and fleshier than the remainder. The left inguinal ring admits the tip of the finger for a distance of 2 cm. The right inguinal canal containing the tumor mass is very large. The appendix is stretched out and elongated by the tumor growth, to which it adheres; it is 15 cm. long. The tumor fills the entire retroperitoneal tissues from the dome of the diaphragm, which it pushes up, down into the pelvis. Everywhere it is covered by a smooth fibrous capsule and shows no tendency to infiltrate. Everywhere it is pale, often watery and semifluctuating, but nowhere cystic or hemorrhagic. It yields no slimy or mucinous material. There are areas of lobulated fatty tissue passing directly into the edematous fibrous tumor tissue; also, there are areas where the tissue is more fleshy and slightly pinkish. The several types of tissue seem to be separated into distinct lobules, generally from 4 to 10 cm. in diameter. The right kidney and adrenal are embedded in the tumor mass, but not adherent; left kidney and adrenal not embedded. The mesentery is invaded slightly, but still leaves a free mesentery about one-half the normal length. Intestines free and nowhere adherent. There is only a little of the tumor tissue in the pelvis, although it follows the external iliaes along the brim of the pelvis and passes through the right inguinal canal. The pancreas is free from the tumor. Omentum not involved and lesser peritoneal cavity is empty and free from adhesions.

Pleural Cavity. Both pleural cavities are free from adhesions and contain very little fluid.

Pericardial Cavity. The pericardial cavity contains a small amount of clear fluid. The pericardium is smooth.

Heart. The heart is normal and weighs 300 grams. The coronaries are thick-walled and tortuous. The aorta is free from sclerosis and is not surrounded by the tumor mass, which lies mostly anterior to it. The pulmonary arteries are normal. Both iliac arteries are surrounded by tumor masses. The vena cava is somewhat compressed, but there are no thrombi. Just above the bifurcation the sides of the vessel are compressed and adhesions of apposed intima have formed, completely occluding the left common iliac vein, but it contains no thrombi. The portal vein contains no thrombi.

Lungs. The lungs are small and collapsed. The right lung weighs 500 grams and there are no nodules in the lung or pleura. The lower lobe is boggy and semisolid. The left lung is more boggy than the right and weighs 850 grams. It is full of turbid fluid except the anterior margin of the upper lobe. The cut surface shows grayish areas, with central softening and gray consolidated areas. The pleura above these areas is not roughened.

Peribronchial Lymph Glands. The peribronchial lymph glands are very anthracotic, but not greatly enlarged. One on the right side shows a gray caseous area.

Liver. The liver is crowded up with the diaphragm, the dome of which reaches the lower border of the first rib on the right side and the lower border of the second rib on the left side. The liver has no relation to the tumor except for adhesions about the right lobe and the peritoneum over the tumor. The liver weighs 1800 grams. The right lobe is increased slightly and the left lobe is atrophied in the outer half, where it is reduced to a layer 3 to 7 mm. in thickness. The gall-bladder is slightly enlarged. The common bile duct is not distended. The cut surface of the right lobe is of a grayish color. There is a well-defined solid area in the middle part of the right lobe, wedge-shaped, 6 cm. wide and 6 cm. deep. It is dark in color and shows autolysis, but there are no thrombosed vessels in this area. The cut surface of the left lobe shows loss of hepatic tissue, with connective tissue remaining.

The spleen, adrenals and pancreas appear normal.

Gastro-intestinal Tract. The stomach is normal. The descending colon and sigmoid are about twice the normal length and stretched about the tumor. There are dense adhesions between the colon and the tumor, and there is great edema in the vicinity of the hepatic flexure. There is great induration of the fibrous tissue about the cecum. The appendix is greatly elongated by a tumor mass between it and the cecum.

Kidneys. The kidneys weigh 300 grams. Both are firm and pale and the cortical markings in both are obscure. The veins about the left ureter are greatly distended, but the ureter is not distended. The right kidney is deeply embedded in tumor tissue, which does not infiltrate or adhere. The capsule on each strips easily, leaving a smooth surface. The ureters and urinary bladder appear normal.

Generative Organs. The right testicle is soft, large and flattened. There is a marked atrophy of the glandular tissue, but there is no change in the epididymis. The left testicle has increased fluid in the sac. It is large and the glandular tissue is normal. The right seminal vesicle contains fluid, but the left seminal vesicle is empty. The prostate appears normal.

The lymph glands of the abdomen show no enlargement or other abnormality.

Muscular System. There is a marked diminution of muscular tissue throughout the body.

Skeleton. The vertebral column is normal and not involved by the tumor growth. The ribs flare out at the base.

Anatomical Diagnosis. Retroperitoneal, edematous fibro-liposarcoma; slight ascites; compression of both lungs, with hypostatic edema of right lower lobe and left upper lobe; acute hypostatic and aspiration pneumonia of the left lower lobe; upward dislocation of heart; pressure atrophy of the left lobe of liver; occlusion of the left common iliac vein by compression and adhesion; edema and varicose veins of both lower extremities; early varicose ulcers of the right

leg; chronic edema of the external genitals; tumor mass in the right inguinal canal; fibrosis of the right testicle; recent laparotomy wound; fibrocaceous right peribronchial lymph gland; enlargement of the chest cavity; recent phlebotomy wound of the right elbow; emaciation.

Histological Examination. The tissues outside the tumor showed nothing of particular interest, corresponding in all respects to the gross findings. No signs of metastatic growth or tumor cell emboli were observed. The chief findings in the tumor itself were as follows: Histologically the tumor shows the same degree of variation that

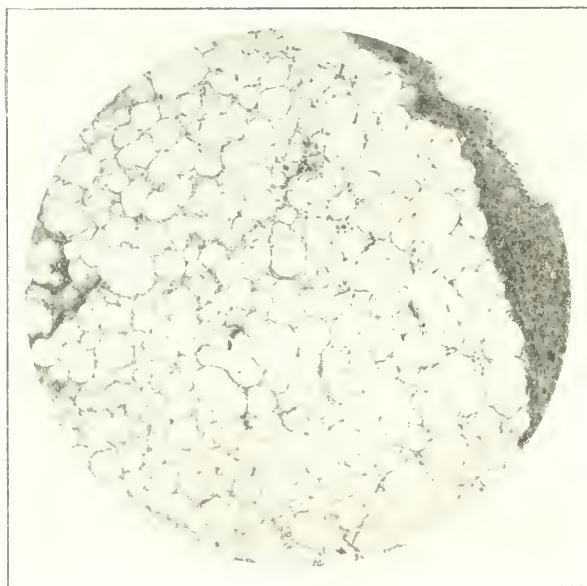


FIG. 3.—Fatty portions of tumor, showing fat cells greatly distended with fat, in contrast with the completely exhausted condition of the normal fat deposits shown in Fig. 6. In the stroma elements irregular and abnormally large nuclei will be seen. $\times 60$.

it does to the naked eye. There are areas that seem to be composed of pure fatty areolar tissue, but even in the parts that most closely resemble a benign lipoma there is occasionally found in the interstitial tissue a large deeply staining and altogether abnormal nucleus (Fig. 3). This is also true of the well-defined fibrous capsule that surrounds all parts of the growth, even in the areas where it is covering the most typical fat tissue. The more solid fleshy portions of growth consist of a structure that in most respects resembles an ordinary fibrosarcoma, but always more or less atypical (Fig. 4). The edema of the intercellular substance and the tendency for the appearance of multinucleated cells and atypical cells, with

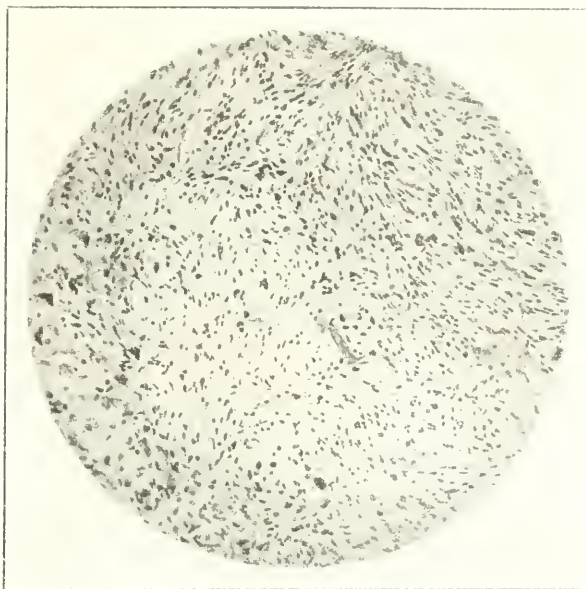


FIG. 4.—Fibrosarcomatous tissue which makes up the bulk of the tumor. Note the numerous exceptionally large and irregular nuclei. $\times 110$.

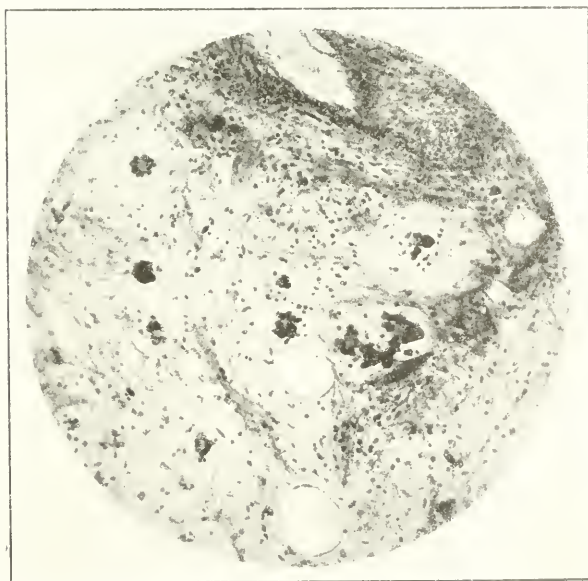


FIG. 5.—Showing the edematous tumor tissue, and the multinucleated cells which are conspicuous in this growth. $\times 110$.

single, large, irregular and often bizarre nuclei, are marked features (Fig. 5). All possible transitions between the fat tissue and the solid fibrosarcoma are seen. A large proportion of the tumor consists of fat cells, with excessive amounts of fibrous tissue containing varying numbers of abnormal cells.

It is to be noted that the fat cells are almost always fully distended with fat, and do not present at all the appearance of fat tissue that has given up its fat for metabolism. This is in marked contrast with the structure of the normal fatty areolar tissues elsewhere in the body, which show almost complete disappearance of the fat deposit, to about as extreme a degree as is possible, as shown in Fig. 6.

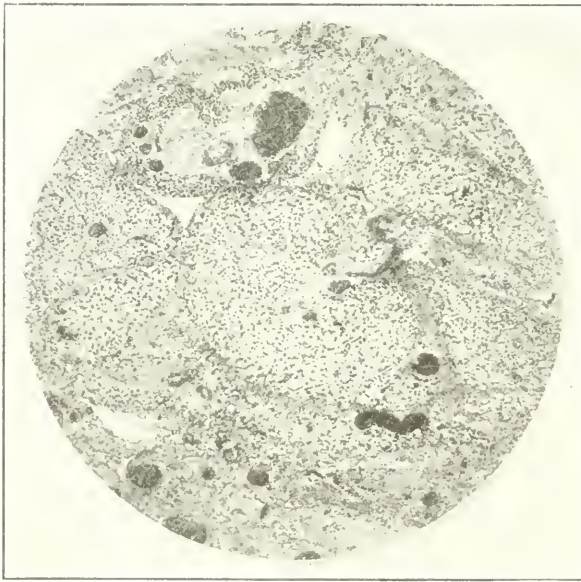


FIG. 6.—Fatty areolar tissue about the adrenal. Illustrating the completely exhausted state of the fat cells, which contain practically no fat whatever. Compare with Fig. 3, showing the fatty tissue of the tumor magnified to the same degree. $\times 60$.

The giant cells are extremely varied in their structure (Fig. 5). The commonest form exhibits a small cluster of deeply staining nuclei, ten to twenty of which appear in a single plane. Often these nuclei appear at the periphery, resembling somewhat a Langhans giant cell, but differing essentially in the exaggerated size of the nuclei, their intense staining and the relatively large proportion of the giant cell that they form. In some, however, the nuclei of the giant cells are in the center, often with a greatly vesiculated cytoplasm. Mitotic figures are not seen, but many nuclei give

the impression of direct division. In some areas numerous small round cells are present and also many cells with a small dark nucleus and nearly homogeneous eosinophile cytoplasm.

The collagen fibers are well developed and made conspicuous by the edema of the tissue. Bloodvessels are usually well developed and in places are extremely numerous, although, for the most part, the degree of vascularity is not different from that of ordinary fat tissue. There are but few polynuclear leukocytes. There are considerable areas of the tumor where very few nuclei are seen although large amounts of stroma substance remain. In the vicinity of these areas there are usually few of the large atypical cells, and the impression is created of a degeneration of the tumor tissue from the lower blood supply. Nowhere is there found any material resembling mucin in its basophilic properties. While sometimes cells with branching processes occur, they do not have the typical mucoid matrix about them, and hence they resemble the stellate cells commonly seen in edematous fibrous tissues. These microscopic observations agree with the absence of any appreciable quantities of material behaving in solubility like mucin.

It is to be remarked that in this tumor we have found no evidence of mucin or so-called myxomatous tissue. The growth is essentially a highly edematous fibro-lipo-sarcoma.

The microscopic difference between this tumor and tumors properly designated as lipomamyxomatodes is very distinct, and emphasized by comparison with sections from a tumor of the latter type in our collection. This specimen was brought to the laboratory many years ago, with the statement that it was a lipoma which had been removed from the right Scarpa's triangle of a woman, aged forty years. It had been present for three years and had shown rapid growth only in the two months preceding the operation. The growth had a distinct capsule and was readily shelled out. It resembled an ordinary lipoma in being lobulated and fatty, but was much softer than a lipoma, very watery, with a slimy fluid escaping from the cut surface, which was extremely pale, with a boiled-starch appearance. It was nearly spherical, approximately 15 x 13 x 10 cm.

Microscopically the tissue everywhere consists of an intimate mingling of fat cells and myxoma cells, with an abundant mucoid deposit possessing marked basophilic properties. There is an absence of edematous connective tissue or of giant cells and other sarcoma cell types. However we were informed that there was rapid recurrence after the operation with early death.

CHEMICAL COMPOSITION. Samples were taken from different parts of the tumor tissue removed at autopsy, as nearly as possible securing a fair average of the tumor as a whole, and these samples were united and analyzed.

Extraction with $\text{Ca}(\text{OH})_2$ yielded but a trace of material precipi-

tating on acidification with acetic acid, indicating the absence of any considerable quantity of mucin.

The figures obtained are given in the following summary, together with the figures obtained by analyzing a typical old granulation tissue, as existing in the so-called "castration tumors" in swine. These great granulomas are quite common, apparently resulting from a chronic infection of the operation wounds. Histologically they consist for the most part of dense fibrous tissue, with few cells and a scanty blood supply.

	Fibro-liposarcoma.	Granuloma.
Alcohol ether residue	6.53 per cent.	15.84 per cent.
Alcohol ether extract (dried)	2.94 "	2.28 "
Total solids	9.47 "	18.12 "
Water	90.53 "	81.85 "

ALCOHOL ETHER RESIDUE.

Total protein	669.1 mgm. per gm. solids	911.6 mgm.
Protein sulphur	6.5 mgm. "	3.3 mgm.
Protein phosphorus	4.4 mgm. "	3.1 mgm.
Total purin nitrogen	1.3 mgm. "	0.7 mgm.

ALCOHOL ETHER SOLUBLE.

(a) EXTRACTIVES.

Total inorganic (ash)	61.3 mgm. per gm. solids	19.2 mgm.
Total solids	129.2 mgm. "	66.4 mgm.
Total sulphur	1.2 mgm. "	0.5 mgm.
Inorganic sulphur	0.3 mgm. "	trace
Total phosphorus	1.5 mgm. "	0.9 mgm.
Inorganic phosphorus	1.3 mgm. "	0.7 mgm.
Total nitrogen	7.9 mgm. "	3.4 mgm.
	49.0 mgm. protein	21.9 mgm. protein.

(b) LIPINS.

Total nitrogen	1.7 mgm. per gm. solids	0.9 mgm.
Total sulphur	1.3 mgm. "	0.5 mgm.
Total phosphorus	1.9 mgm. "	0.9 mgm.

The analysis shows that we are dealing with an edematous fibrous tissue rather than with a myxoma, as shown by the presence of 90.53 per cent. of water and no appreciable mucin. The other figures merely confirm the fact that this tissue is more embryonic in character than the granuloma, as indicated by the greater amounts of sulphur, phosphorus and purin nitrogen.

The figure for fat was lower than anticipated, showing that the lipomatous elements did not form so large a proportion of the tumor as the gross appearance suggested. Nevertheless, there was present nearly two pounds of fatty material and four and a half pounds of protein in this tumor, despite the extremely emaciated condition of the host. Both microscopic and chemical examination afford striking evidence that a malignant tumor can retain considerable

amounts of fat under conditions in which the normal fat depots give up almost their last molecule of fat.

SUMMARY. There is reported the microscopic and chemical examination of a retroperitoneal liposarcoma without myxomatous elements, weighing sixty-nine pounds, being the largest solid tumor of which we can find record. It illustrates the capacity of malignant tumors to store up protein and fat, despite extreme emaciation of the host.

VASCULAR REACTIONS IN VASCULAR HYPERTENSION.¹

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A STARTLING observation, made two years ago, was directly responsible for the following study:

The patient was a woman, aged forty-eight years, with an extremely high blood-pressure and a normal renal function, one of those cases familiarly known as "vascular hypertension." Her systolic pressure had just been found to be 270, when the patient complained of rather severe cardiac pain. Nitroglycerin, gr. $\frac{1}{100}$, was given for relief. Curiosity led me to watch its effect on the blood-pressure. I was very much disturbed to find the pressure falling rapidly until it reached 110. In the meantime the patient had become very uncomfortable and was almost in collapse. An intravenous injection of adrenalin restored the pressure as quickly as it had fallen, and the patient became more comfortable.

This observation was so amazing that I was stimulated to study the reaction to nitroglycerin of the bloodvessels in this type of case. (I should state, at this point, that the above observation was unique on my part, none of its kind having since been made.) In the course of the investigation on the effect of nitroglycerin it was noted that during the preliminary period of our experiments, while we were trying to establish a base line before giving the drug, there was often a marked fall in pressure, due to rest and quiet. If exciting noises occurred near the patient, however, the pressure often rose to a surprising degree. The variations in pressure were so marked that we were led to determine not only the effect of nitroglycerin but also that of rest, excitement, exercise and afterward adrenalin. These results were interesting and instructive enough to warrant this report.

While some of the earlier experiments were, for obvious reasons,

¹ Study made under a grant from the Proctor Fund of Harvard University.

not done under standard conditions, the majority of those reported were carried out in the following manner: The patient was placed in bed in a quiet room for twenty to forty-five minutes. The object of this was to put him at his ease. At the end of this preliminary period the systolic and diastolic pressures and the pulse-rate were noted at five-minute intervals. Usually these patients established their base lines in thirty to forty-five minutes. Then I endeavored to excite the patient by urging him to talk about some disturbing subject. Generally his "high blood-pressure" (on which most of these patients are terribly centered) or his irritability, or some similar subject, was a sufficient excitation. It would, perhaps, have been somewhat better to have some standard form of excitation, such as that used by Meakins and Wilson in their study on "Irritable Heart,"² but no such means seemed practical or necessary. During the short two- or three-minute period of excitation, readings were again made and then the patient was allowed to become quiet again. After a sufficient time had elapsed to re-establish the base lines the effect of exercise—usually lifting from a reclining position to a sitting one ten times—or the effect of nitroglycerin under the tongue was tried. The adrenalin test was carried out in a similar way on another day. The doses of the drugs are given in the tables. Each observation consumed from one and a half to three or more hours on two days.

The first reaction to consider—the effect of quiet and rest—can be followed in Table I.

Here it can be seen that in the large proportion of the cases there was a definite and marked fall in both systolic and diastolic pressures during the preëxcitation period. In a very few, however, there was essentially no fall. In the systolic pressure the variations in the curves ranged from 0 to 46 mm., with an average of 21 mm. In the diastolic the fall varied from 0 to 18 mm., with an average of 10 mm. The time necessary to establish such falls varied markedly, as did the degree of fall, both being largely dependent on the nervous tension of the patient. The limits were from five to seventy minutes.

I presume that the following sequence of events took place in these patients. In spite of the preliminary rest period many were very nervous when the blood-pressure was first determined. As a result the pressure rose above its previous undetermined level. As the patient became accustomed to this maneuver the pressure fell. That this was true is indicated by the fact that the second and third readings were occasionally higher than the first. These were followed by the usual fall.

The effect of excitement showed a greater change in the pressure curves in the opposite direction. In every case there was a sharp rise. This was generally greater than the corresponding fall in the

² Heart, 1918, No. 1, vii, 17. In this study a pistol shot was used as a means of excitation.

preliminary period. The variations in the systolic pressures ranged from 10 to 52 mm., with an average of 30 mm. The diastolic pressures showed similar but less marked rises varying from 8 to 24 mm., with an average of 12 mm. In general, the rise was a very sharp one, the height of pressure being reached at the first determination. In some there was a rise at this reading, but the curve continued to ascend, reaching its maximum in ten to fifteen minutes.

TABLE I.—EFFECT OF REST AND EXCITEMENT IN VASCULAR HYPERTENSION.

Med. No.	Blood-pressure at start.		Maximum fall in mm. due to rest.			Maximum rise in mm. due to excitement.			Stimulus.
	Syst.	Diast.	Syst.	Diast.	Time in min.	Syst.	Diast.	Time in min.	
8022	126	98	3	18	40	10	8	5	Talking about a quack.
53819	148	92	30	16	65	24	8	15	Talking about father's death, etc.
7761	150	84	10	4	70	24	10	10	Talking about self and school work.
11704	152	98	14	2	20	34	24	15	Talking about blood-pressure and operation.
10664	172	98	18	2	20	40	10	5	Talking about her family.
6596	186	98	-1	5	30	20	8	5	Talking about her invalid daughter.
8976	186	110	0	0	—	52	10	5	Talking about her irritability.
8920	192	98	12	0	5	28	9	10	Thinking of a dead pet cat.
9799	198	99	23	10	40	—	—	—	Rest only.
9799	202	80	46	18	50	28	16	5	Talking about her school.
7608	209	92	35	10	60	50	10	5	Talking about her divorce.
8742	214	128	14	8	25	19	10	5	Talking about blood-pressure.
9846	222	122	—	—	—	36	8	10	Talking about self.
9846	227	122	19	12	20	32	24	15	Talking about blood-pressure.
6877	230	108	27	14	30	28	12	5	Talking about an attack of angina.
11581	238	104	26	1	65	16	9	10	Talking about blood-pressure.
Extremes	0-46	0-18	5-70	10-52	8-24	5-15	
Average	21	10	..	30	12		
						Controls.			
Manuel	114	64	4	4	10	10	14	5	Talking about exam.
F. Smith	116	62	6	2	20	14	6	5	Talking about exam.

In this and subsequent tables some of the cases do not seem to be hypertensive. They are, however, patients who have been many times hypertensive. By "time in min." is meant the time elapsed in reaching the maximum rise. The averages at the bottom of the table are only of those showing a positive rise. Two normal cases are included at the bottom of the table for comparison.

The effect of exercise in these hypertensive cases (Table II) showed somewhat conflicting results, as in normal cases. In general there was a fairly definite rise in both systolic and diastolic pressures. In one there was no rise in either. In two more there was a fall in the systolic and in five there was a fall in the diastolic pressure. The usual type of curve was a sharp rise followed by a fall almost as sharp. Rarely this is reversed. The results are similar to what occurs in normal individuals. The psychic element undoubtedly

plays a part in the reaction. The results are of special interest, however, in that they show how marked and how sudden a change may take place in these hypertensive patients as a result of moderate effort. A rise of 57 mm. in a normal patient is of much less significance than in a patient who already has a high pressure. (See Case No. 6596.)

TABLE II.—EFFECT OF EXERCISE.

Med. No.	Blood-pressure before exercise.		Maximum rise from exercise.		
	Systolic.	Diastolic.	Systolic.	Diastolic.	
53849	120	70	0	0	
8533	128	—	—4	—	
10664	132	84	10	—6	
7761	140	92	20	—2	
11704	142	100	16	0	
9799	162	80	26	8	
7608	168	82	45	0	Somewhat tired.
9799	170	80	42	4	
6596	184	98	57	22	
8976	186	120	10	—4	Tired.
10032	194	112	32	18	
8742	202	118	8	4	
6877	218	104	30	18	Tired.
8846	222	122	—20	—10	On repetition later; no fall in pressure from exercise.
Extremes	—20 70	—10—22	

It is of interest to note that while the diastolic pressures in the above experiments were more stable than the systolic they were far from being fixed. A variation of 24 mm. in the diastolic pressure within a two-hour period is indeed surprising. (See Case No. 8846, Table I.)

The observations recorded above may be merely exaggerations of what occurs normally. But in the hypertensive case they are of vastly greater significance. Furthermore the recognition of the fact that such wide variations in pressure can occur within a comparatively short period due to such commonplace causes as those used, is of extreme importance in estimating the meaning of any given high pressure. It must, too, make us very cautious about the interpretation of the effects of treatment. If a patient's pressure under the influence of mental and physical rest can drop 35 mm., and then under the excitation of talking about family difficulties can rise again 50 mm. (see Case No. 7608, Table I; see also same case, Table II) one can readily understand the wide variations that must take place every day in this type of case. One can understand, too, of how little significance are even moderate changes noted from time to time unless they are all in the same direction.

As a result of such observations as these I have become very skeptical about the therapeutic value of drugs, electricity, baths, etc., in this type of case. If they produce any effect at all it is largely through the accompanying mental or physical rest imposed.

Unless one can show a permanent or at least a long-continued lowering of pressure of a considerable degree, one cannot rightfully claim that any given therapeutic maneuver has been beneficial. I have yet to see a fall in pressure resulting from any method of treatment (except rest) that cannot be duplicated or exceeded by those observations we have made on rest. By the latter means one may reduce the pressure markedly, but, unfortunately, on the resumption of effort it rises again. However, with care it need not rise to its former level. After all, this is as much as we should reasonably expect, except in the earliest cases.

Another thought arises out of this study. The extreme liability of the vasomotor system in this type of case, as indicated by the marked and sudden changes in pressure, makes us wonder what the effect on the vessels must be. Will not these patients show earlier and more marked sclerosis of the vessel walls?

TABLE III.—EFFECT OF NITROGLYCERIN.

Med. No.	Blood-pressure at start.		Primary rise in mm.		Primary fall in mm.		Secondary fall in mm.		Time in min.	Dose in G.		
	Systolic.	Diastolic.	Systolic.	Diastolic.	Systolic.	Diastolic.	Systolic.	Diastolic.				
53819	148	92	4	0	—	—	—	2	16	15	0.0006	Slight reaction.
11704	152	95	22	22	—	—	—	2	0	30	0.0009	
10664	154	100	20	2	—	—	—	22	18	35	0.0009	
6596	186	98	20	4	—	—	—	5	6	35	0.0009	
8976	186	110	14	16	—	—	—	18	8	30	0.0009	
9799	188	99	24	11	—	—	—	19	14	50	0.0009	
9767	190	112	19	10	—	—	—	3	2	15	0.0006	
7608	209	92	26	10	—	—	—	22	8	45	0.0009	
6877	230	108	11	21	—	—	—	6	0	20	0.0009	
9106	238	154	5	16	—	—	—	25	0	20	0.0009	
10962	288	172	10	—	—	20	—	15	20	—	10	
7761	128	92	—	—	16	12	23	—	—	—	0.0009	Some doubt about diast. pressures
9767	190	112	—	—	2	2	5	-8	-10	15	0.0006	
8920	196	120	—	14	28	—	14	60	31	244	0.0006	
8880	212	102	—	14	32	—	23	—	4	—	0.0006	
11581	238	104	—	12	22	—	7	—	—	—	0.0009	

This table is divided into two parts. The first 11 cases are those which showed a primary rise. The others showed a primary fall. The last three in the second group showed no primary rise in the systolic pressure but a rise in the diastolic. One case in the first group showed a rise in systolic pressure and a fall in the diastolic.

In studying the effect of nitroglycerin in this disease we received two genuine surprises (Table III). Instead of finding a sharp fall of pressure after a fairly large dose of this drug placed under the tongue we found that the majority of our cases showed a primary rise. This, too, occurred during the height of the symptomatic reactions to the drug. The patient was flushed. There was pounding in the head and in the region of the heart. The radial pulses were definitely more full, and yet the systolic and diastolic pressures

were higher at this period instead of lower. Furthermore, these rises were not always trifling, being over 20 mm. in several cases. I am of the opinion that in these strikingly nervous people the excitement produced by the nitroglycerin caused the primary rise.

The second surprise was in the comparatively slight depressor effect of the drug. The drop in pressure, either following the primary rise or when there was no such rise, was comparatively slight. I say this in spite of the apparent contradiction in Table III. If one notices those cases in which a considerable fall took place after the nitroglycerin, he will see that, for the most part, it required a very long time to reach this depth. I cannot help feeling that much of this fall must be attributed to rest and quiet, otherwise, it seems to me, we should obtain the greatest drop during the period of vasodilatation, *i. e.*, during the period of flushing, increased pulse volume, etc.

Observations like these confirm our ideas about the uselessness of nitroglycerin in hypertension. Formerly we discarded this drug on the grounds that the depressor effect was too transient to be of value. These experiments of ours show that there is but little reduction of pressure due to the drug and that there is often a primary rise in pressure. Rest alone is far more effective.

TABLE IV.—EFFECT OF ADRENALIN.

Med. No.	Blood-pressure at start.		Maximum rise in mm.		Time in min.	Duration of rise.	Dose in c.c.	Remarks.
	Syst.	Diast.	Syst.	Diast.				
7761	132	90	42	50	2	20	0.5	
8533	134	48	48	10	10	45	0.5	Plateau curve.
53819	140	80	30	12	2	60	0.5	Rather prolonged rise.
11701	160	104	80	-40	2	25	0.5	Sharp, marked rise.
10664	166	98	52	10	2	22	0.5	Double rise.
7608	194	90	10	10	24	120	0.5	Slow rise and fall; typical syndrome reaction.
6877	199	94	70	22	5	40	0.5	Double rise; angina.
8976	200	120	26	10	10	15	0.25	Too small a dose.
6596	206	101	87	22	2	95	0.5	Sharp rise and fall, the latter trailing off; angina.
8846	211	118	8	-2	2	5	0.5	? about site of injection.
Extremes	26-87	10-50	..	15-120		
Average	53	18				
					Controls.			
Manuel	111	62	8	2	4	55	0.5	Normal student.
De Blois	100	60	11	10	2	50	0.5	Gastric necrosis.

Only 2 normal cases are included at the bottom of the table for purposes of comparison. For normal controls, see report of work at Lakewood.

In spite of the above, nitroglycerin has a place in the treatment of one of the complications of vascular hypertension. Clinical experience has taught us its value in angina pectoris. In the light of our results one cannot help wondering about the effect of this drug on the various bloodvessels of the body. There is no doubt that it

causes a vasodilatation of many of the vessels. This can be seen and felt. No doubt, too, in angina the relief comes from such a vasodilatation, and yet there is a compensating or overcompensating mechanism in this disease which maintains the pressure at a high level in spite of the nitroglycerin.

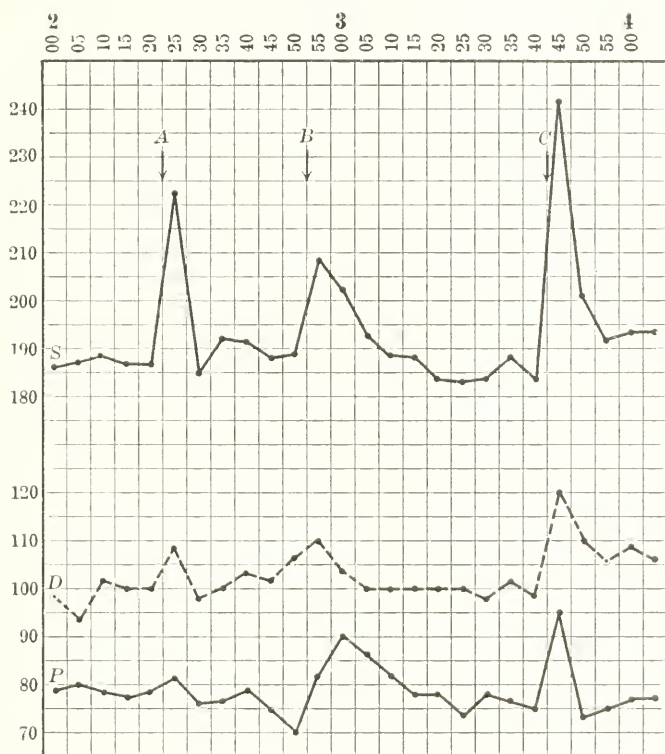


CHART I.—In this chart and those that follow, the ordinate indicates time, the abscissa, pressures, pulse and respiration rates. *S*, systolic blood-pressure; *D*, diastolic blood-pressure; *P*, pulse-rate; *R*, respiration-rate. In the diastolic pressure curve the symbol \circ is occasionally used. This indicates that no abrupt change from a sharp to a muffled note was heard but merely a gradual decrease in sounds. The \circ represents the level at which the last sound was heard. Chart I demonstrates the effect of emotion, nitroglycerin and exercise. At *A* is noted the effect of talking two minutes about an invalid daughter. At *B* nitroglycerin, 0.0009 G., was given under the tongue. Note especially the rise of 20 mm. in the systolic pressure and the comparatively negligible fall of this pressure. At *C* the patient lifted herself from the reclining to the sitting position ten times.

One of the most interesting phases of this study of ours is that of the effect of adrenalin, as in the Goetsch test.³ Sturgis and Wearn,⁴ at Lakewood, have shown that $\frac{1}{2}$ c.c. of a 1 to 1000 solution of drug given intramuscularly in normal individuals causes no appreciable rise in blood-pressure.

³ New York State, Jour. Med., July, 1918, xix, 259.

⁴ Arch. Int. Med. September, 1919, xxiv, 269.

Our data is very meager consisting of only ten cases. This small number is due to the fact that we became afraid to use the drug in this type of case. The reaction was so striking and so nearly constant that we feel it worth while to report our cases. In only one case (No. 8846, Table IV) did we fail to get the typical reaction. In this one case there was some doubt about the technic.

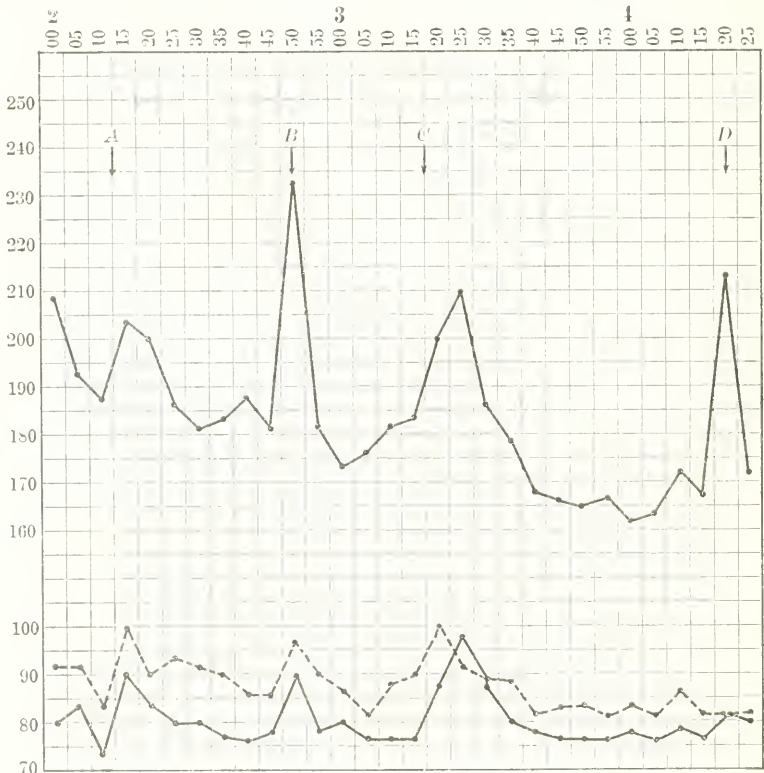


CHART II.—This demonstrates the effect of emotion, nitroglycerin, and exercise. At *A* the patient was stirred up while her pressure was apparently falling, by placing a blanket on her chest. At *B* can be seen the effect of talking two minutes about her divorce. At *C* nitroglycerin, 9.0009 G., was given under the tongue. At *D* can be seen the effect of lifting herself from the reclining to the sitting position ten times.

The technic was almost identical with that used by Sturgis and Wearn⁵ at Lakewood, the only difference being that we used the prepared solution of adrenalin, whereas there a solution was made from tablets. The patient was kept at rest in bed in a quiet room for one-half to one hour. Control pressure readings, pulse and respiration rates, symptoms, etc., were then noted at five-minute intervals until a base line was established. Then $\frac{1}{2}$ c.c. of a 1 to 1000

⁵Sturgis and Wearn, cited above.

solution of adrenalin was injected into the deltoid or biceps muscle. Pressure readings, etc., were thereafter made every two minutes for ten minutes, then every five minutes for one hour or more, and then every ten minutes until the pressure came back to normal.

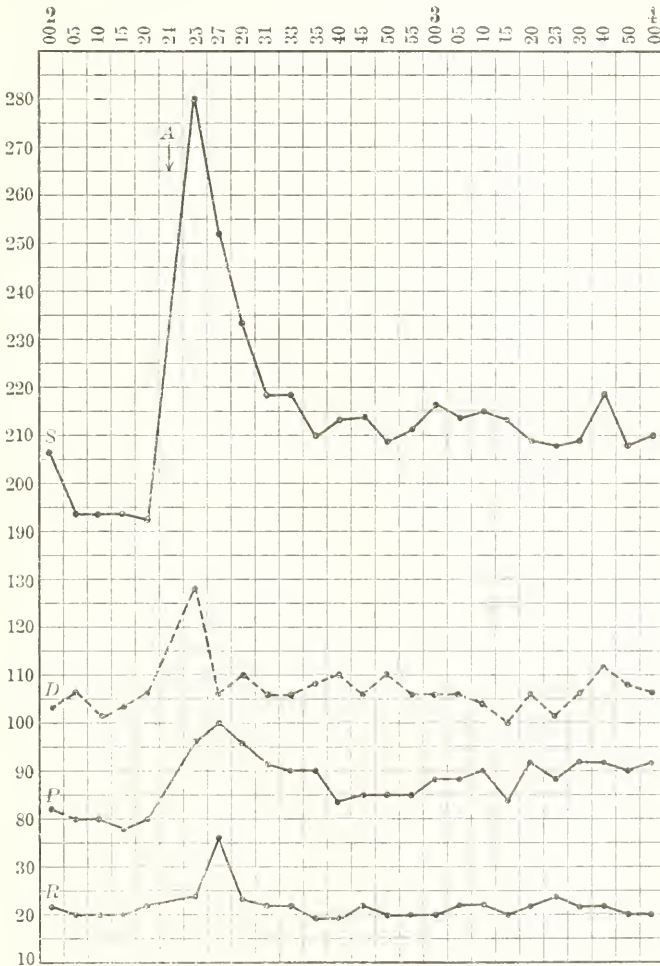


CHART III.—This demonstrates the effect of adrenalin. At A the patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Note the sharp, terrific rise in pressure.

The reaction to the drug was striking and in some instances alarming. A typical one showed a sharp rise of pressure averaging 53 mm. for the systolic and 18 mm. for the diastolic. In two cases the maximum systolic rise was over 80 mm. When such a rise took place within two minutes after the drug was injected it was indeed striking, especially if it started from a base line of over 200 mm.

Generally the pressure was not maintained at the high level for longer than a few minutes. It then fell, sometimes fairly abruptly and sometimes more gradually. Occasionally there was a secondary slight rise during the fall. The time required to reach the maximum pressure and to reach the former level is indicated in Table IV. Immediately after the injection of the drug the patient became pale



CHART IV.—Another adrenalin effect. At A the patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Patient had severe angina pectoris.

and tense and had a feeling of tingling all over. There was sometimes a slight tremor of the hands and usually a pounding in the head and in the region of the precordia. In one or two there were practically no symptoms.

Neither in the symptomatology nor in the pressure curves did our cases resemble those of the "effort syndrome" reported from Lakewood. Only one case (No. 7608, Table IV) showed the typical "syndrome curve," but this patient did not display the symptoms which are so characteristic.

A few of the curves resemble more closely those reported by Goetsch in his hyperthyroid series, especially those with the secondary rise (Nos. 10664 and 6877, Table IV). As a rule, however, our cases showed a much more abrupt and higher rise than did those of Goetsch. That these patients were cases of hyperthyroidism is not at all credible. In fact, we have determined the basal metabolism on a few that seemed possibly thyrotoxic and found it to be subnormal instead of raised.

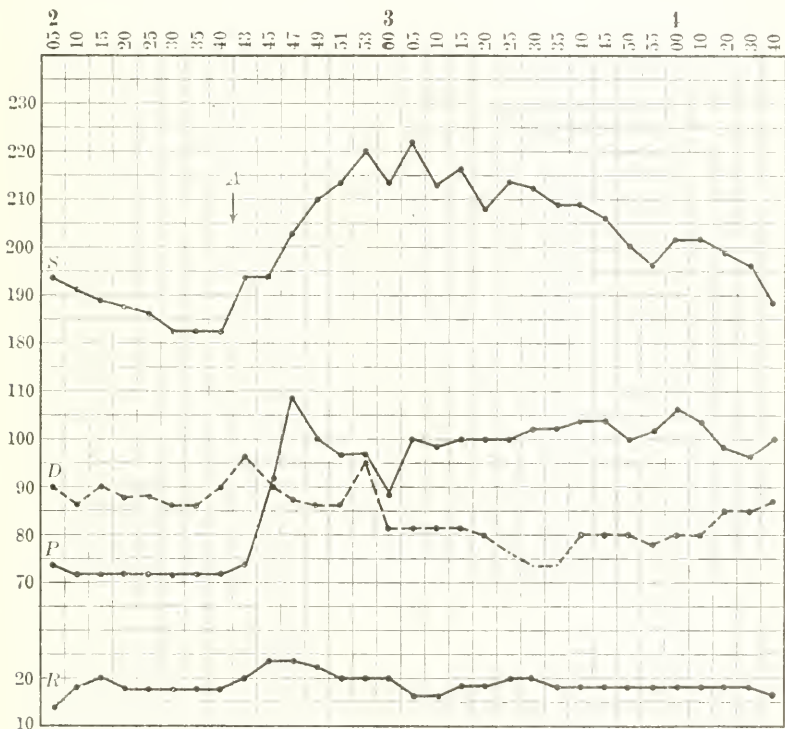


CHART V.—Another adrenalin effect. At .1 patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Note the more slow and sustained rise in pressure. This resembles the reaction obtained by Goetsch in his hyperthyroid cases.

Two cases in this series warrant special comment because of the alarming nature of the reaction. Case No. 6877 was an elderly woman who had had several attacks of rather mild angina pectoris. After the injection of adrenalin the pressure rose immediately 70 mm. The patient became very pale and frightened and had the worst attack of angina she had ever experienced. Fortunately the pressure fell rather promptly and the symptoms abated as quickly.

The second case (No. 6596) showed a similar alarming jump in the systolic pressure from 193 to 280 in one minute. She, too, became very pale and frightened and had a tremendous sense of constriction in the region of her heart.

Both of these patients felt they were going to die and I was much alarmed. It was a great relief to see the pressure fall instead of continuing to rise.

Cases like these made me unwilling to try this reaction further in patients with a pressure over 190 mm. Consequently my series is small. They should serve as a warning against indiscriminate use of adrenalin intramuscularly.

The "adrenalin reactions" in hyperthyroidism, the effort syndrome and in vascular hypertension are interesting problems requiring much more study. In the last group the worker must realize that he is "playing with dynamite."

It is safe to conclude from these studies that:

1. The vasomotor system in vascular hypertension is extremely labile and sensitive.
2. Mental and physical rest causes a marked fall in pressure.
3. Excitation causes a more marked abrupt rise.
4. Exercise usually causes a similar rise.
5. Nitroglycerin produces practically no fall in pressure and there is often a primary rise following its absorption.
6. The vessels are especially sensitive to the intramuscular injection of adrenalin, a marked rise in pressure taking place immediately after its injection.

I gratefully acknowledge the assistance of Miss Elsa Griffin.

THE DANGERS OF ASCARIASIS.

BY BOWMAN CORNING CROWELL, M.D.,

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ANIMAL parasites of the human host are today probably attracting more attention than ever before, while with improved modern methods new ones are being discovered, and, as the result of accumulated knowledge, pathogenic properties are being ascribed to those formerly considered harmless. The technic of the laboratory is being employed in all its refinements to aid in diagnosis, and, on the other hand, treatment of some forms of intestinal parasitism is being carried out on a more scientific basis and on a larger scale than could have been foreseen only a few years since. International campaigns against parasites are now taken in a matter-of-fact way, and the mention of their scope in all their vast inclusiveness excites little more than passing admiration.

Probably greater efforts have been expended against the hook-worm, the malarial parasite and the entameba than against the other animal parasites. But who ever gives a thought, other than one of disgust, to the *ascaris*? And yet the wide territory covered by the *ascaris*, the number of the population infested by it and the harmful results attending its presence entitle it to more respectful attention than is usually accorded it. In practically all places, if not in all, in which examinations are made for parasitic infections it is found that the *ascaris* is the parasite most frequently encountered. It is also one of the worms that is most easy of recognition, and for that reason very little difficulty attends the diagnosis. Perhaps these facts have helped to distract the interest of the physician from this homely worm. The average physician who has had any experience in tropical countries where the *ascaris* abounds will say that the treatment of ascariasis is easy, which is probably true in the vast majority of cases, and that its harmful effects are slight anyway, which is decidedly not true. It is my opinion that the word of the pathologist on this subject is heard only too infrequently, and it is for this reason that I wish to put on record some of my experiences with this worm as seen in the autopsy room during several years in Manila. This experience has led me to look upon the *ascaris* with more than the usual amount of respect and fear. The pathologist and the medical man who follows his cases to their ultimate diagnosis are better qualified to speak on this subject than the pure parasitologist or the man who knows only mortality statistics based upon clinical diagnosis alone. A simple examination of the hospital records of tropical countries will show what a large number of cases are admitted to these hospitals for ascariasis alone, aside from those in which ascariasis is found complicating other diseases which are usually considered more serious. If this be followed by an examination of the records of the associated morgues, with their never-ending list of surprises, the case against the *ascaris* will be strengthened. I regret not being able to give accurate statistics on this subject, but I know that they would convince even the most skeptical that this parasite has a very decided economic importance as judged from the morbidity caused by it.

As the worm is a large one and easy of recognition, much attention was paid to it by the earlier workers on this subject, and some of the older books on parasitology give a better idea of the importance of this worm than one would acquire from a perusal of some of the more modern works. The average medical student at present is therefore sent out into practice with an erroneous idea concerning the importance of this disease. Fortunately, attention has recently been again directed to this worm through the work which is being done on the method of transmission of the parasite, and it therefore seems an opportune time to once again draw attention to the harm attending infestation by it.

Fantham, Stephens and Theobald,¹ in their recent book, *Animal Parasites of Man*, and Blanchard,² in his *Zoologie medicale* of thirty years ago, give excellent ideas on the pathology of ascariasis, and frequent references will be made to these works.

PREVALENCE OF THE PARASITE GEOGRAPHICALLY AND IN MAN. Documentary evidence will not be given here to bear out the statement that the *ascaris* is more widely distributed from the geographical standpoint and infests a larger number of people than any other known intestinal parasite. Text-books, monographs, hospital and morbidity records all agree upon this point and place it beyond all possibility of dispute.

My personal experiences with ascariasis were chiefly gained in the Philippine Islands, and I shall quote a few statistics from there to show its incidence. Willets,³ in 1911, found 62.3 per cent. of 4278 persons infested with *ascaris* as compared with 54.37 per cent. with hookworm, and in a grand total of 19,302 examinations compiled by the same author in the Philippines, 61.36 per cent. had *ascaris* and 30.57 per cent. had hookworm. In some of the series from which these statistics were compiled the percentage of *ascaris* infestations was as high as 83. In 500 consecutive autopsies on cases the majority of which came from a hospital in which routine treatment for intestinal parasites was practised, Crowell and Hammack⁴ found 41.2 per cent. with *ascaris* as compared with 16.6 with hookworm. In other places the incidence of the *ascaris* runs up to almost 100 per cent.

The *ascaris*, unlike many other parasites, does not confine itself to the tropics, but is found in all climates and in all latitudes.

PATHOLOGICAL EFFECTS OF THE ASCARIS. The pathological effects of the *ascaris* are numerous, but are susceptible of classification.

I. Mechanical effects are prominent and certain from the *ascaris*; these may be exerted when the worm is in the intestine or in the course of its migrations.

II. As a carrier of infection the worm is also of importance in its migrations. Whether through its eggs it may prove a source of transmitting infection is not yet proved.

III. The larvae cause a bronchopneumonia in experimental animals, and it is not improbable that they may do so in some cases in infants.

IV. The presence of a harmful toxic substance is a source of danger and reflex nervous symptoms due either to mechanical or toxic irritation are also frequently encountered. These phenomena will now be dealt with in more detail.

¹ *Animal Parasites of Man*, 1916, John Bale, Sons & Danielsson, Ltd., London.

² *Traite de Zoologie medicale*, 1889, J. B. Baillière et Fils, Paris.

³ *Philadelphia Jour. Sc.*, Sec. B, 1911, vi, 77.

⁴ *Ibid.*, 1913, viii, 157.

I. MECHANICAL EFFECTS OF THE PRESENCE OF THE ASCARIS.

1. *In the Intestine.* Large numbers of the worms may be present in the intestine; one individual has been reported to have evacuated as many as 600 worms in one day and other large numbers are frequently reported. Fauconneau-Dufresne is quoted by Blanchard as having published a case in which a boy, aged twelve years, evacuated more than 5000 worms in less than three years, the majority by vomiting; 600 were evacuated in one day only!

In our autopsy experience as many as 200 were found in the intestine of one child, and numbers from 50 to 75 were so frequent as to occasion no surprise. Such masses of these worms may cause not only constipation but absolute obstruction. Fantham, Stephens and Theobald credit cases of ileus to Mosler and Peiper, Raic, Rehberg, Rocheblave, Leichtenstern, Huber and Wilms.

The collection of large coils of the worms in the sigmoid flexure of the colon may cause palpable, firm masses in the left abdominal quadrant, which have led to the clinical diagnosis of true tumor of the intestine. This is a frequent source of error to newly arrived physicians in the tropics, and I have seen an abdomen opened under this false diagnosis. Vermifuges have caused many a prospective operation for suspected abdominal tumors to be indefinitely postponed.

The question as to whether the *ascaris* actually may perforate the intact wall of the intestine or stomach is still open. Certainly the worm is often found in the peritoneal cavity at autopsy. Some authors quoted by Blanchard attributed this wholly to the parasites, whether they produce the perforations or determine foci of gangrene. Others maintain that the perforations occur independently of the worms, and that they simply use an exit which they find available; and still others maintain that the worm is capable of passing through the intestinal membrane by simply separating the fibers; its passage completed these fibers come together again, owing to their elasticity and contractility, and all trace of the perforation disappears. Blanchard collected a total of 81 cases in which the *ascaris* had passed out through the body wall, especially at the umbilicus and groin. Davaine points out that these exits of the *ascaris* are more frequent at the umbilicus in children and at the groin in adults, corresponding to the frequency of hernia at the two places. They have also been reported as having been passed through the urethra with the urine, and here it may be supposed there was fistulous connection between the bladder and the intestine.

Other wanderings of the worm have been described in which it would seem that the worm had passed through tissues. It seems probable that exact anatomical investigations would increase the number of cases in which it would be found that these cases are explicable on the basis of fistulous openings in the tissues through which the worms may pass. These fistulas may remain patent or

close after the passage of the worms. The predilection that these worms have for passing into small orifices is well known and frequently emphasized. Thus, Clason⁵ records that in the case of an idiot whose custom it was to swallow glass beads the *ascarides* showed a predilection for sticking in the beads and were passed in the feces. Blanchard refers to the fact of the worms engaging themselves in the holes of buttons that have been inadvertently swallowed, and says that certain authors have even proposed objects of this kind as worm snares. This habit of the worms was exemplified on one of our cases in which a full-grown *ascaris* had penetrated through the tunnel in the submucosa, connecting two adjacent tuberculous ulcers of the colon, and was found protruding from both ulcers and doubled on itself so as to form a knot.

I have seen the *ascaris* in the peritoneum at autopsy many times after cases of rupture of the intestine, and in some cases when there was a postmortem digestion of the stomach, which made an easy exit possible. More interesting are the cases of perforative appendicitis or diverticulitis through which the worm has passed to the peritoneum. Several cases of perforation of the appendix occurred in our autopsy service in which *ascarides* were present in the peritoneum. It is natural to suppose that they had passed out through the opening in the appendix, but this does not indicate that they were the cause of the appendicitis. I have notes of four appendices removed surgically which contained the *ascaris*, and in none of these was there evidence of severe disease in the appendix. These cases are as follows:

A Filipino woman, aged thirty-two years, had the appendix removed incidental to the removal of a large multilocular cyst of the ovary. The appendix contained an *ascaris* but showed no pathological change. A similar case was seen by me in New York ten years ago.

A Filipino woman, aged twenty-seven years, had the appendix removed incidentally to a cholecystectomy; it contained an *ascaris*, and slight atrophy of the mucosa was present.

A Filipino woman, aged forty years, had the appendix removed under the diagnosis of chronic appendicitis; its lumen contained a portion of an *ascaris* and two trichurides; slight catarrhal changes only were present.

An American child, aged seven years, had the appendix removed under the diagnosis of acute appendicitis. The appendix measured 7.5 cm. in length and about 7 mm. in diameter; the superficial blood-vessels were markedly congested and the lumen contained an *ascaris*. Microscopically there was seen only a slight atrophy of the mucosa.

In the latter 2 cases, and in other similar ones that I have seen, it is probable that the appendicular symptoms would have been

⁵ Quoted by Fantham, Stephens and Theobald.

transitory. The reason for my mentioning these cases is to emphasize that the presence of the *ascaris* in the appendix does not necessarily lead to severe changes in the appendix, and also that symptoms simulating appendicitis may be caused by their presence. It is, however, probable that the pain is the most prominent symptom and that a temperature record with a blood count and examination of the feces might clear up the diagnosis. Another case illustrating another point in this connection will be reported.

A male Filipino of four and a half years was autopsied seven and a half hours after death. The abdominal cavity contained about 50 c.c. of thick, greenish, creamy pus and the coils of intestine were matted to one another by delicate fibrinous adhesions. The coils of the small intestine were much dilated and the serosa was pale except in the areas covered by the fibrin. Lying free on a coil of the small intestine next to the anterior abdominal wall to the left of the umbilicus was a small *ascaris*. Other *ascarides* were found enmeshed in the adhesions, especially in the region behind the transverse colon and over the region of the left kidney. There were in all eight living *ascarides* found free in the peritoneal cavity. Over the region of the left kidney one coil of intestine presented a diverticulum which had perforated. This was situated in the ileum at a point 30 cm. from the ileocecal valve, and originated from the lateral aspect of the intestinal wall nearer to the mesenteric attachment than to the opposite side. At its tip were two small perforations covered with fibrin. It is not necessary to suppose that the perforations were caused by the *ascaris*, but it is very easy to imagine that they might have determined a perforation in an inflamed diverticulum, and it is certainly true that their passage from the diverticulum prevented the circumscribing of the inflammatory phenomena by the usual process.

I have had several cases in which the *ascaris* had actively opened up a repaired wound of the intestine, thus determining a fatal peritonitis. This emphasizes the importance of the routine examination of the feces and the use of vermifuges if *ascaris* is found in all cases of abdominal operations of choice. It is unfortunate that this is a precaution often omitted even when *ascaris* is known to abound. Of course there are cases in which vermifuges are contraindicated and cases in which operation is urgent. In these cases precautions appropriate to the individual case should be taken. I will here report one case that I have had among others illustrating this danger.

No. 5695. A male Filipino, aged thirty-seven years, received a severe blow on the abdomen from a "push-cart." He was taken at once to hospital, where intestinal rupture was found and repaired by end-to-end anastomosis. Death ensued eight days after operation and autopsy was performed six hours after death. The following extract is made from the autopsy protocol:

On the abdomen, at the margin of the right rectus muscle, between the umbilicus and pubis, is a long surgical incision enclosed by sutures. From the lower end of this there protrudes a gauze and rubber drain. On removing the sutures the margins of the skin are easily pulled apart, and on separating these margins the subcutaneous tissues are found to be necrotic and bathed in foul-smelling pus. The sutures below the skin have separated and a loop of intestine presents in the abdominal wound, forming its base. This loop of intestine is intimately adherent to the anterior abdominal wall by fibrin. On opening into the abdominal cavity the entire left side of the abdomen is found free from exudate. On the right side the loops of small intestine are adherent to the anterior abdominal wall and to one another. The intestine in the upper part of the abdomen is markedly dilated. A loop of small intestine is present in the middle of the right side of the abdomen, with its surfaces closely adherent to one another. On separating these adhesions an opening in the intestine is found which had been closed by sutures. From this opening fecal matter pours and two dead *ascarides* lie on the mesentery adjacent to this opening. The great omentum is pulled downward and to the right, and is adherent by fibrin over the matted intestine. On loosening the loops of the intestine and cecum from the right abdominal wall there is found a large collection of pus which fills the lower right quadrant of the abdomen and extends into the pelvis. Between the middle portion of the ascending colon and the right abdominal wall there is found a dead *ascaris* lying on the mesentery just behind where the duodenum pierces the mesentery. In both of these places fibrin is piled up from the peritoneum about the *ascarides*, almost enclosing them, so that when the worms are removed the groove of fibrin on the peritoneum remains. On separating all the adhesions of the intestine and mesentery and removing them it is found that the intestine is dilated down to within about half a meter of the cecum, and below this it is collapsed. The opening in the intestine is at a point $2\frac{1}{2}$ meters from the pylorus. Here an end-to-end anastomosis has been performed, but the margins were separated. In the upper intestine brown, watery fluid is present and about a dozen *ascarides*. In the collapsed lower intestine there is abundant, dry, sticky feces and some trichurides are found in the cecum.

Interest attaches to the presence of the *ascarides* in the peritoneum and the reaction of the peritoneum to their presence as has been described above. At the time of operation fecal matter was present in the abdomen and the peritoneum was thoroughly flushed with salt solution. It is a question whether the *ascarides* entered the abdomen before or after operation. The absolute localization of the extensive peritonitis to the right side of the abdomen is also of interest, as is the point of rupture of the intestine. It is extremely probable that the peritoneum was thoroughly cleaned at the opera-

tion and that subsequently the *ascarides* had forced their way between the sutures, thus causing the fatal peritonitis. The reaction of the peritoneum about the worms proves that this was not a case of postmortem migration. Microscopically ova of *ascaris* were abundant in the peritoneal exudate.

2. *Outside of the Intestine.* When, at autopsy, the *ascaris* is found outside of the intestine there is frequently some difficulty in determining whether the migration occurred before or after death. Unless there is some clinical evidence before death of the *ascaris* being outside of the intestine I have made it a rule to consider the migration to have occurred after death, except in those cases in which there is evidence of reaction to the presence of the worm or when the worm is in such a condition or position that it obviously could not have attained after death. For instance, in the case just reported there was no doubt that the migration was antemortem on account of the piling up of the fibrin about the individual worms. The presence of the *ascaris* in the larynx or trachea after death has not been accepted by me as evidence of the cause of death unless other evidences such as those caused by asphyxia were also present. At times dead worms are found in the bile ducts or in other positions when the short period elapsing between the death of the patient and the autopsy has rendered obvious the antemortem occurrence of the migration. Such considerations are of great value in leading to correct interpretations of the autopsy findings.

Migration to the Bile Channels and Liver. Migration of the *ascaris* into the common bile duct and thence into the gall-bladder or into the intrahepatic bile ducts is a frequent occurrence, and must be much more frequent than is indicated by the reported cases, as the diagnosis is made only at operation or at autopsy. One of several worms may pass through the papilla of Vater in this way, and may cause occlusion, followed by icterus, with the symptoms of colic, or may lead to the development of a cholangitis and later abscesses of the liver. Thus the action of the worms in the bile ducts may be either purely mechanical or they may serve as carriers of infection into the liver. Leer⁶ says that *ascarides* are the second most frequent cause of liver abscess. Vierordt⁷ states that mature females can penetrate into the liver and there deposit eggs, and that such eggs appear occasionally to undergo segmentation. The worms may be found in the ducts alive or dead, and may show constrictions about the body when they have become strangulated by pressure.

After the death of the worms in the bile ducts they become macerated and flattened, stained with bile, and may become encrusted with bile pigments, as is shown in cases 3422, 2387, 2524, 3192, 3905. (See below.)

⁶ British Med. Jour., 1916.

⁷ Volkmann's Samml. klin. Vortr., No. 375.

The abscesses in the liver are usually multiple and the pus within them very foul. They may perforate in any direction and the worms may be evacuated through the opening formed. Communication of the abscesses with the bile ducts is usually readily recognizable on account of the dilatation of the ducts caused by the passage of the worms. If the abscesses be seated near the periphery of the liver adhesions may form between the liver and the adjacent tissues. In Case 1007 a subdiaphragmatic abscess had formed and the base of the right lung was adherent to the diaphragm, with a localized empyema. Lebert is quoted by Blanchard as having seen a liver abscess extend through the diaphragm and lung and evacuate itself through the bronchi, as sometimes occurs in cases of hepatic amebiasis. It is to be remembered that *ascarides* may migrate into the ducts of a liver which is the seat of abscesses from other causes.

In one of our cases to be reported (424) there were three large *ascarides* in the hepatic ducts, the largest of which extended to the surface of the right lobe of the liver. The common duct was distended and practically occluded by the folded bodies of two full-grown *ascarides*, and one protruded from the papilla of Vater. There was thrombosis of the splenic vein along the pancreas and an acute hemorrhagic pancreatitis, with fat necrosis, without the presence of a worm in the pancreatic duct. It can only be a matter of conjecture in this case whether the pressure of the hilus of the liver from the worms in the ducts led to the venous thrombosis to which the pancreatitis was secondary or whether the pancreatitis resulted from the occlusion of the opening of the pancreatic duct into the common duct, and the thrombosis was a sequel to this.

Reports of some of our cases of migration into the bile passages follow:

CASES OF ASCARIS IN BILE DUCTS AND LIVER.

5684. *Ascarides* in intestine, stomach, esophagus, bile ducts and liver; probable asphyxia from *ascaris*; icterus.

A little flaxen-haired American-Filipino "mestizo" of four years was known to have *ascarides* and had undergone home treatment. One morning about a week after treatment had ceased he was taken *suddenly* with jaundice and sweating, both of which became intense. Within five hours he was in hospital and not apparently in a very serious condition; he was put into bed and the father left him to find the physician. Upon the father's return with the physician within five minutes the child was found dead. Autopsy was performed within two hours of death. There was no evidence of status lymphaticus. The skin had a decided icteric color. The blood was dark and not coagulated; the lungs were distended and there was a frothy fluid in the bronchi, trachea and larynx. The larynx was edematous. There were small epicardial and pleural hemorrhages. The duodenum was distended with numerous *ascarides*, which

formed a compact mass throughout its entire length, and there were numerous *ascarides* in the jejunum. The bile ducts were distended with five large *ascarides*, which extended into both hepatic ducts, obstructing the flow of bile. These living *ascarides* extended nearly to the surface of the liver. There were numerous *ascarides* in the stomach and six large ones in the esophagus. The only lesion found in the other viscera was congestion.

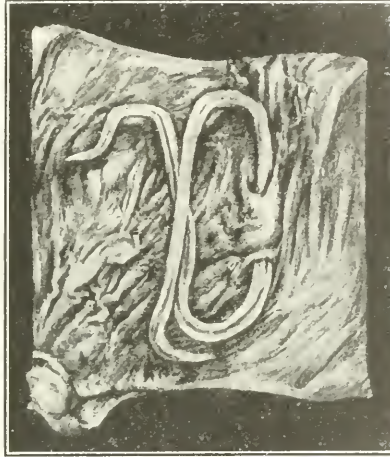


FIG. 1.—*Ascaris* tunnelling between two tuberculous ulcers of colon.

There appear to be two possible explanations of the sudden death in this case: (1) Reflex nervous phenomena from intestinal and biliary ascariasis, or (2) what seems more probable, asphyxia from *ascarides* in the upper respiratory tract. It is true that there were no *ascarides* found in the respiratory tract at autopsy, but the esophagus was filled with them, the larynx was edematous and there were other signs of asphyxia as noted above.

4424. *Ascarides* in stomach, hepatic and common bile ducts; hemorrhagic pancreatitis; thrombosis of splenic vein; fat necrosis.

Female, Filipino, aged thirty years. Duration of illness, two days. No jaundice; 100 c.c. of blood-tinged fluid in peritoneum. Very abundant extravasation of blood, behind the peritoneum, in pancreas and lesser peritoneal sac. Liver weighs 1255 grams and is of normal size. The hepatic duct contains three large *ascarides*, the largest of which extends to the surface of the right lobe of the liver. The common bile duct is distended and practically occluded by the folded bodies of two full-grown *ascarides*, and one protrudes from the papilla of Vater into the duodenum. The gall-bladder is considerably distended and contains brick-red, thin bile.

The pancreas lies in its normal position and is surrounded by a very hemorrhagic serous membrane. The pancreatic duct is free

and opens into the common bile duct, about 5 mm. above the papilla. The accessory duct is not seen. The splenic vein running along the pancreas contains a long thrombus, which is adherent to the posterior wall of the vein and seems to extend into the branches of the splenic vein leading into the substance of the pancreas. The body and tail of the pancreas are dark red, considerably softened and somewhat friable. The cut surface shows bright purple to dark red soft lobules which are separated by dark red septa. In some areas the lobules are yellowish, very soft, with intensely hemorrhagic zones surrounding them. The head of the pancreas is firm, pale and its cut surface shows light, yellowish, clearly outlined, firm lobules. On the surface of the capsule are seen a few grayish-white to yellowish-white, flat, pin-head-sized areas, which are also seen on the surface of the mesentery and omentum. Three large *ascarides* in the stomach.



FIG. 2. — Living and dead ascarides in intrahepatic bile ducts, liver and gall-bladder.

3422. *Ascarides* in bile ducts, stomach and intestine; multiple abscesses of the liver.

Female, Filipino, aged five years. Duration of illness, one month. Autopsy performed nine and a half hours after death. Death from pulmonary tuberculosis.

The liver is slightly enlarged. The greater part of the surface is smooth and yellow. The right anterolateral margin is reddened and firmer than the adjacent tissue for a distance of 3 or 4 cm. from the edge. On the anterior surface within this area are two small elevations, each about 1.5 cm. in diameter, which are yellow and fluctuating. Scattered over the remainder of the superior surface are a few, small, reddish, non-elevated areas which are softer than the sur-

rounding tissue. The greater part of the left lobe is reddened and increased in consistence. On the inferior surface, near the tip, is a small, soft, yellow elevation, and extending from this toward the hilum of the organ is an elevated, mottled, yellowish-red ridge. On the superior surface is another small, yellow elevation to which a little fibrin is adherent.



FIG. 3.—Liver abscesses resulting from ascarides in bile ducts.

On opening the duodenum about two-thirds of a long *ascaris* is seen projecting from the orifice of the common bile duct. The orifice is closed by the worm, but the duct above it is markedly dilated and contains parts of other *ascarides* which extend up into the liver. The mucosa of the duct is smooth but reddened. Both the right and left branches of the hepatic duct are dilated and filled with *ascarides*, those in the left branch causing the ridge seen on the surface of the left lobe.

The yellow areas on the surface overlie small abscess cavities which connect with the bile ducts, but are closed, or partially closed, by *ascarides*. The parenchyma in the reddened areas surrounding the abscesses and dilated bile ducts is moist and friable; elsewhere it is soft, yellow and greasy.

The worms are not confined to the main branches, but extend into

the smaller ducts and into the abscesses. The total number of parasites present is between fifteen and twenty, it being impossible to count them without removing them from the liver. The majority of the worms are well preserved and apparently alive, though motionless; but on both the right and left side are found one or two which are dead, macerated and bile-stained. The largest measures about 18 cm. in length.

The cystic duct is slightly dilated. The gall-bladder is not enlarged and contains turbid, light green bile. Its mucosa is bile-stained and not reddened. Three *ascarides* in stomach and seventy-eight in intestine.

2387. *Ascarides* in bile ducts; cholelithiasis; cholangitis; cholecystitis; abscesses of liver.

Male, Filipino, aged forty years. Duration of illness, two days. Autopsy performed seventeen hours after death.

The gall-bladder is enormously distended, projects about 5 cm. beyond the costal margin and measures in its distended state about 10 cm. in its lateral diameter. On palpation of the common duct a firm mass is felt in its lower portion. On opening up the common duct an opening is found in the duodenum, which is considerably larger than the normal opening of the duct, and on closer examination the true orifice is found about 1.5 cm. from this, the first opening representing a fistula. About 1 cm. back of this fistulous opening are two brownish stones, one large (1.2 cm.) and the other small; these have not entirely obstructed the duct, however, since bile could be pressed from the gall-bladder before the duct was opened. Just back of these stones lies a brownish, coiled-up mass which is found to be an extremely long *ascaris*, which is flattened and covered with deposits of bile pigment. The mucosa of the duct at the point where the stones lay is hyperemic and shows two or three small greenish-colored, shallow ulcers; back of this point it is markedly dilated as is the hepatic duct and its branches. No other stones are found except a small one in a branch of the hepatic duct. The gall-bladder contains a thin, rather sticky fluid, which is fairly clear but contains occasional yellowish or brownish particles. The mucosa of the gall-bladder is intensely hyperemic, and scattered over it are numerous shallow ulcers, which are stained a deep green color, so that at first they seem to be small patches of membrane.

The liver is large; on the surface are seen several yellowish dots, most numerous on the left lobe. On section of the right lobe the ducts are seen to be greatly dilated and in one of them, and apparently attached to its wall, lies an *ascaris*; the worm is in a good state of preservation, though apparently dead at this time; near it in the duct is another worm. Scattered here and there through the liver substance are small, yellowish areas, 2 to 4 mm. in diameter, and in the vicinity of many of these there is evidently an increase of connective tissue; these areas are infrequent in the right lobe, but

on section of the left lobe are found more often. The remaining liver parenchyma is reddish brown and rather friable. No *ascarides* were found in the intestine or stomach.

2524. *Ascarides* in bile ducts, gall-bladder and intestine; abscesses of liver.

Male, Filipino, aged five years. Autopsy two hours after death. Died of tuberculosis.

The liver, about normal in size, is firm and of a yellowish color. On the diaphragmatic surface are seen four well-defined abscesses of a yellowish-green color, averaging about 1 cm. in diameter, fluctuating on pressure. On the inferior surface of the right lobe is a linear abscess about 2 cm. long and 0.5 cm. wide, of a greenish color. None of these abscesses has penetrated the capsule. The organ cuts with decreased resistance; the cut surface is yellowish and dry. The lobulations are not distinct. The abscess cavities are well defined and apparently communicate with the larger bile passages, which contain living and much disintegrated dead *ascarides*. The liver weighs 575 grams.

The gall-bladder is much distended with green bile and contains two large living *ascarides*. The mucosa shows no gross change. Many *ascarides* in intestine.

2797. *Ascarides* in bile ducts, small intestine and stomach; abscesses of liver.

Male, Filipino, aged one year and seven months. Interval between autopsy and death unknown. Died of Asiatic cholera.

The left lobe of the liver looks red and inflamed. Upon section this portion is found to contain a dead *ascaris* within a bile duct, which is dilated and contains a small amount of yellow fluid. Around this duct are seen many small pale areas, irregular in outline, about 1 to 5 mm. in diameter; some are larger. These areas are soft and structureless in the centers. Around the periphery the liver tissue is red and swollen. There is another *ascaris*, which is alive in a branch of the hepatic duct. The surface of the liver is smooth. The organ is soft. It presents a dull, gray, mottled appearance. Many *ascarides* are present in the small intestine and stomach.

1007. *Ascarides* in bile ducts, liver, intestine, stomach and esophagus; abscesses of liver.

Male, Filipino, aged five years. Duration of illness, one month. Autopsy performed on day of death.

Multiple abscesses in liver up to 4 cm. in diameter. One large abscess on dome of right lobe, its upper wall formed by the diaphragm. Abscesses contain greenish, foul-smelling pus and *ascarides*. Common bile duct, hepatic duct and intrahepatic bile ducts and abscesses filled with *ascarides*. General suppurative peritonitis apparently originated from the subdiaphragmatic abscess. Base of the right lung was adherent to the diaphragm and there is here localized empyema and gangrene of the lung. Gall-bladder free. *Ascarides* also present in ileum, cecum, stomach and esophagus.

1929. *Ascarides* in bile ducts, stomach and intestine; fluctuating projections on the surface of the liver. Case of sudden death in a subject of status lymphaticus.

Male, Filipino, aged five years. Duration of illness, thirty minutes. Autopsy performed the day after death.

Liver weighs 720 grams. Common bile duct, hepatic and intra-hepatic ducts are much dilated and contain numerous *ascarides*. These extend from hilum to capsule. Fluctuating projections on the surface of the liver, but no actual abscesses described. Ten to twelve *ascarides* in stomach and numerous in intestine. Base of right lung adherent to diaphragm.

3192. *Ascarides* in bile duct, pancreatic duct and intestine; bile duct dilated.

Male, Filipino, aged forty-two years. Duration of illness, two days. Autopsy performed sixteen hours after death. Died from transverse myelitis and fracture of the seventh cervical vertebra.

In the hepatic and common duct is found a dead *ascaris* folded on itself; one end of it macerated and bile-stained. The bile duct is slightly dilated, but otherwise is apparently normal. A large *ascaris* has penetrated the pancreatic duct to a depth of about 8 cm., the worm projecting into the duodenum. The worm is still living. No lesions of the pancreas are made out. A few *ascarides* are present in the intestine.

3905. *Ascarides* in bile ducts and intestine; abscesses of liver and pancreas; cholelithiasis; icterus; hemorrhages.

Male, Filipino, aged seventeen years. Duration of illness, four days. Autopsy performed twelve hours after death.

Jaundice is present. There is hemorrhage into the peritoneal sac without recognizable source of origin. There is also abundant, altered blood in the intestine, stomach, mouth and nose, which may have originated from the necrotic ampulla of Vater. Extensive hemorrhages are present in the retroperitoneal tissues, about the kidneys, in the pelvis, in the subserous coat of the jejunum and in the subpleural tissues. The liver is enlarged and weighs 1661 grams. It shows many small abscesses from 3 to 8 mm. in diameter, containing green pus. The common bile duct is 4.5 cm. in circumference and contains nine greenish black faceted smooth stones. Four dead and decomposed *ascarides* are found in the common and hepatic ducts and their branches. There is also much pus in the pancreas, especially near its tail. Its ducts are dilated but do not contain bile. The gall-bladder is dilated and contains dark green bile. There are forty-two living *ascarides* in the intestine.

3579. *Ascarides* in bile ducts, gall-bladder and intestine; possible postmortem migration.

Female, Filipino, aged five years. Duration of illness, fourteen days. Autopsy performed eighteen hours after death. Died of Asiatic cholera.

Liver is about normal in size. Located in the right hepatic duct, entering into the substance of the liver for a distance of about 4 cm., there is an *ascaris*. This *ascaris* is curled upon itself in the hilus of the liver and the other half enters into the left main hepatic duct for a distance of about 2 or 3 cm. Located in the gall-bladder and common bile duct there is an *ascaris*. The gall-bladder contains, besides the *ascaris*, a small amount of thin, turbid, greenish bile. "*Ascarides* are present" in the intestine.

2896. *Ascaris* in cystic duct; dilatation of gall-bladder.

Male, Filipino, aged four years and one month. Autopsy performed nine hours after death. Died of acute malaria.

Gall-bladder is distended, forming a large, sausage-shaped, cystic mass, with thin wall. It contains some golden yellow, very thin bile. A living *ascaris* is present in the cystic duct, its head extending up into the gall-bladder, and its tail is just at the point of junction of the cystic and common ducts. The common duct is not dilated. No mention is made of other *ascarides* in the intestine.

MIGRATION TO THE PANCREAS. Worms may pass into the duct of Wirsung and determine either the formation of abscesses or the development of an acute hemorrhagic pancreatitis. It also seems probable that the *ascaris* in the common bile duct may so block it as to lead to the development of an acute hemorrhagic pancreatitis without the entrance of the worm into the duct of Wirsung.

CASES OF ASCARIS IN PANCREAS.

Cases 4424 and 3905 have been already described along with the cases of *ascaris* in the bile ducts and liver.

4582. *Ascarides* in pancreatic duct and intestine.

Female, Filipino, aged forty years. Duration of illness, one year. Autopsy performed sixteen hours after death. Died of tuberculous pneumonia.

The only pertinent note is that an *ascaris* was found in the pancreatic duct and there is a slight hemorrhagic area at the tail of that organ. Numerous *ascarides* in the intestine.

2478. *Ascaris* in pancreatic duct and intestine; probable post-mortem migration.

Female, Filipino, aged seventeen years. Duration of illness, thirteen days. Autopsy performed sixteen hours after death. Death from acute endocarditis and myocarditis.

The only pertinent note is that the pancreas shows a large *ascaris* well engaged in the duct of Wirsung. Pancreas shows no change. Few *ascarides* in the intestine.

MIGRATIONS OF THE ASCARIS TO OTHER PARTS. The migration of the *ascaris* to the stomach and esophagus and thence to expulsion through the mouth or nose is extremely frequent. If fistulous tracts are encountered *en route* the worm may reach unusual places.

It may also pass into the accessory nasal sinuses, antrum of Highmore, lacrimal duct, Eustachian tube and external ear or into the larynx and trachea. In one of our cases a live *ascaris* was found in the middle ear of a child after death.

Passage of the worm into the larynx may cause suffocation, and numerous cases are quoted by the authors already referred to in which removal of the worm from the larynx or trachea had led to the disappearance of alarming symptoms. The precaution has already been suggested of hesitating to ascribe harmful effects to the presence of *ascarides* found in the respiratory passages after death unless signs of death by asphyxia are present.

Case 5684 described above illustrates the effects of *ascaris* in the respiratory passages.

II. THE ASCARIS A CARRIER OF INFECTION IN ITS MIGRATIONS. This subject needs only to be appreciated. The way in which infection has been carried to the peritoneum, liver, gall-bladder and pancreas, giving rise to suppurative inflammation in these places, has already been exemplified in the above cases and constitutes one of the serious dangers of ascariasis.

III. BRONCHOPNEUMONIA IN THE COURSE OF ASCARIS INFECTION. Stewart⁸ and Ransom and Foster,⁹ in their studies on the life history of *ascaris* in experimental animals, have found that a bronchopneumonia may develop and may prove fatal, if the infection is massive, from the presence of the larvæ in the lungs of these animals (pig, rat, mouse and guinea-pig). In a case of human experimental infection, Lutz¹⁰ recorded the occurrence of a severe bronchopneumonia in the subject of the experiment during the incubation period. From this it seems not improbable that some, at least, of the cases of bronchopneumonia in infants and children may be due to the presence of the larvæ in the lunge, and thus constitute a hitherto unsuspected danger of *ascaris* infestation.

IV. TOXIC AND REFLEX NERVOUS SYMPTOMS FROM ASCARIS. In the present state of our knowledge it is difficult to speak with any degree of accuracy upon this important and interesting phase of ascariasis. I have grouped together the toxic and reflex nervous effects for purposes of discussion because of their frequent association and the practical difficulty in distinguishing between them. It is probably true that the number of cases of ascariasis which come under this head is immeasurably greater than those which come into the hands of the pathologist, which have been described above. Clinical histories and the therapeutic effects of vermifuges unite to incriminate the *ascaris* as the cause of almost all sorts of toxic and nervous phenomena. Fevers, nausea, flatulence, abdominal pains, convulsions, tetany, symptoms of chorea, hysteria and epilepsy,

⁸ British Med. Jour., 1919, p. 102.

⁹ Jour. Agric. Research, 1917, xi, 395.

¹⁰ Quoted by Stewart.

delusions, hallucinations, psychic disturbances, symptoms simulating meningitis and many other disorders of like nature, which occur in the course of ascariasis and disappear after successful treatment of the ascariasis, come within the ken of those who practice medicine where the *ascaris* abounds. It is therefore logical to ascribe an etiological role to the *ascaris* in these conditions, but the way in which it produces its results is by no means clear.

Flury¹¹ in a chemical and toxicological study of the horse- and pig-*ascaris* found numerous substances both in the body substance and in the excretions which caused local irritation or necrosis. He was able to demonstrate volatile aldehydes of fatty acids and even the free acids, the principal ones being valerianic and butyric acids, and in smaller amounts formic, acrylic and propionic acids, alcohols and esters of the ethyl, butyl and amyl series. All of the symptoms of irritation of the mucous membranes noted by zoologists and the digestive disturbances in ascariasis he attributed to these substances. All of the disturbances of the central nervous system attributed to *ascaris* (hallucination, hysteria, chorea, epilepsy, cramps, tetanus, delusions, psychic disturbances) may be explained on the basis of chronic aldehyde poisoning. A nitrogenous compound was found which caused death, with severe hemorrhages in the intestine after subcutaneous injection in the dog. This was ascribed to its action as a capillary poison. Flury concludes that the *ascaris* produces not a single poison but a number of pharmacologically active substances which may produce very different and at times very severe symptoms.

Shimamura and Fujii¹² have isolated a toxic substance from the horse *ascaris* to which they have given the name *askaron*. This consists of a mixture of albumoses and peptone and gives distinctly toxic symptoms when injected into the horse subcutaneously or intravenously. It is said that this *askaron* is not a specific toxin produced for a definite purpose, but is merely a metabolic substance that happens to be toxic.

Cattaneo¹³ was able to detect only a weak toxin in *ascaris*, while Messineo,¹⁴ by injecting into animals extracts in physiological salt solution, invariably succeeded in producing serious motor disturbances and frequently death.

Whether other toxic effects than those enumerated above can with any degree of probability be ascribed to the *ascaris* is a matter of debate. The pathologist sees many cases of disturbances of the spleen, and to a lesser extent of the liver, which are not accounted for by any of the known etiological agents, and he cannot help wondering whether the *ascaris* by itself or by some change caused by it in the intestine may not play an important role in this respect.

¹¹ Arch. f. exp. Path. u. Pharm., 1912, lxvii, 275.

¹² Saikingaku Zassi, 1916, p. 9.

¹³ Arch. f. Kinderheilk., vol. xlv. Quoted by Fantham, Stephens and Theobald.

¹⁴ Giorn. Med. del regio eserc., 1905. Quoted by Fantham, Stephens and Theobald.

CASES OF ASCARIASIS AND HEMORRHAGES.

3905. See above with "*Ascaris* in Bile Ducts and Liver."

2029. Already published in full by Crowell and Hammack. Briefly, this was an eight-year-old Filipino, who, six days before death, was seized with an attack of vomiting, followed on the next day by pain in the chest and knees. There soon developed external edema, jaundice, melena, hemorrhage from the gums, dyspnea, prostration and ecchymoses on the face and legs. The day before death there were severe anemia, hemic cardiac murmurs, negative Widal reaction, sterile blood culture and no fever. The anatomical diagnosis at autopsy was: ascariasis (150 *ascarides* in stomach and intestine); purpura hemorrhagica; ecchymoses, cutaneous, epicardial, pleural, retropleural, retroperitoneal, gastric and intestinal; partial atelectasis of lungs; anemia; hemorrhage into intestines; trichuriasis; ankylostomiasis.

CONCLUSION. The dangers of ascariasis are liable to be underestimated, and for this reason a number of cases, fatal and otherwise, have been here reported for the purpose of attracting attention to this important subject. These worms may cause symptoms and even death through toxic, reflex and mechanical effects either in the larval stage or while adult in the intestine or in the course of their migrations to other parts of the body. Cases of disease of the intestine or other parts may assume much more than their usual seriousness on account of the presence of these worms, and the accidents due to the migratory proclivities of the worm may cause fatal complications of simple surgical procedures that would otherwise have terminated happily. The number of cases that I have here recorded, which constitutes only a fraction of those I have seen, is not great. It, however, indicates that a thorough and systematic examination of the cases of ascariasis would bring to light as many cases in the experiences of others, and would prove ascariasis to have the importance that I have ascribed to it.

EVIDENCES OF NEPHRITIS AND URINARY ACIDOSIS.

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If the reader of this discussion finds that he cannot subscribe to the title under which I shall treat the present subject, I will beg his indulgence on three points: (1) on the fact that if a specimen of urine were submitted to him for analysis and he found it to contain albumin, blood cells and casts, he could not possibly deny that the individual from whom the specimen was obtained had a neph-

ritis; (2) that such findings are the main evidences of an actual nephritis in all but the late stages of disease; (3) that if such findings occurred in the course of an acute infection, for example, the inference would almost invariably be that a nephritis existed.

I therefore prefer to treat the subject-matter of this paper from the viewpoint of nephritis, because, from such a viewpoint these findings have greater clinical significance, and not because I believe that a true nephritis existed. And also because the acidosis theory of nephritis has up to the present time been neither accepted nor rejected.

PREVIOUS OBSERVATIONS. In an earlier work¹ it was shown that severe and prolonged muscular exertion is accompanied by circulatory disturbances sufficient to cause the presence of blood cells, albumin and casts in the urine. Those observations suggested the inquiry whether anything short of a Marathon race (24.85 miles) would produce similar findings, and the question is answered in the present investigation.

It is interesting to note that an individual who immediately before exercise had a perfectly normal urine will, after forty minutes of exercise, show albumin, red blood cells, hyaline and granular casts. It is indeed surprising to note the rapidity with which hyaline and granular casts are formed in the urinary tubules.

Before going further, I wish to quote a summary of the observations made in Marathon runners:

URINARY FINDINGS BEFORE MARATHON RACE, IMMEDIATELY AFTER
AND AT SUBSEQUENT PERIODS.

	Number of cases.	Albumin.	Blood.	Casts.	Acc. bodies.
Before	24	1			
Immediately after	19	19	18	19	18
One week later	19	19	..	6	
Three weeks later	3	3	..	3	

As will be seen from the above table this inordinate exertion, running a distance of 24.85 miles in a period of 3 hours 14 minutes to 4 hours 15 minutes, produced albuminuria accompanied by blood and casts in all the cases. Five of these showed "showers of casts."

We made also numerous observations on the blood-pressures of those subjects, and in correlating the findings it became evident that albumin occurred in largest amounts in those cases which showed the greatest fall in the maximum pressure and in those which showed most marked falls in the pulse-pressure. Those findings correspond with the studies of Erlanger and Hooker;²

¹ Barach, Joseph H.: Physiological and Pathological Effects of Severe Exertion (the Marathon Race) on the Circulatory and Renal Systems, *Arch. Int. Med.*, 1910, v, 382.

² An Experimented Study of Blood-pressure and Pulse-pressure on Man, *Johns Hopkins Hosp. Rep.*, 1904, xii, 145.

who showed that a direct relationship exists between pulse-pressure and urinary excretion. Later on it was shown by Gesell³ that in the excised kidney, with a given amount of blood, the urinary excretion is greater when the pulse-pressure is larger, diuresis being determined by the size of the pulse-pressure.

The conclusions derived from that study were: From these observations upon the renal functions it seems that the more serious the disturbance of the general circulatory system the more marked are the evidences of this disturbance in the renal circulation. This is shown by the amount of blood and the degree of albuminuria and cylindruria. In these observations no quantitative analyses of the urinary acidity were made.

Since that work, however, it has been stated by Bornstein and Lippman,⁴ who are in agreement with Martin Fisher, that the albuminuria and cylindruria following severe exertion is caused by the increased urinary acidity;⁵ the acid products of increased metabolism irritating the kidneys. This is a most important question in clinical medicine, and we may well bring all of our evidences together for the proper solution of such a problem.

PRESENT STUDY. The following observations were made upon a series of 57 normal young men before and after baseball and daily "try-outs" on the track. These young men were of better than average health, having passed the required physical examination prior to their entrance into the field of competitive sports.

Our observations included the body weight before and after effort, urinalyses before and immediately after, including the amount of urine excreted during the work period, estimation of the hydrogen ion concentration of the urine and examination for albumin, casts and blood cells.

LOSS OF WEIGHT AND URINARY EXCRETION. In the entire series the greatest loss of weight occurred in a subject who weighed 129½ pounds. His loss in 1 hour and 50 minutes of baseball was 5.5 pounds. One subject showed no loss at all and the average loss for all cases was 1.3 pounds. This decrease in body weight was mostly due to loss of water.

The 10 individuals showing the largest amount of urine, and whose average excretion was 87 c.c., lost on an average of 1.55 pounds each, while the 10 whose average was 27 c.c. lost on an average 1.1 pounds each.

DURATION OF THE EFFORT. The average time spent in running was 48.1 minutes. The average time spent in baseball was 1 hour 57 minutes.

³ The Relation of Pulse-pressure to Renal Secretion, *Am. Jour. Physiol.*, 1913, xxxii, 70.

⁴ Weitere Beiträge zur nicht Nephritischen Albuminurie, *Ztschr. f. klin. Med.*, 1918, lxxxvi, 345.

⁵ Gesell, R.: *Loc. cit.*

Taking the first 10 who spent the longest time and the 10 who spent the least time in the exertion the number in which albumin, blood cells and casts were found was exactly the same in both, showing that in this series time element was not a factor.

URINARY ACIDITY. In order to estimate the hydrogen ion concentration, *i. e.*, to estimate the total potential acidity of the urine, we used the method of Folin, which consists of adding a liberal quantity of neutral potassium oxalate to the urine, and then titrating with $\frac{N}{10}$ NaOH, using phenolphthalein as an indicator.

By this method we found that 85 per cent. of all the urines after exercise showed an increased acidity. The actual number of increased acid urines was exactly the same in the baseball cases as in the more strenuous type—the track cases.

The acidity was greater in the 10 cases which showed an average urinary output of 27 c.c. than in the 10 which had an average output of 87 c.c. during the exercise period.

Albumin and casts occurred as frequently in the low acid cases as in the high acid cases.

The average increase in total acidity for the cases showing casts was 16.8—as against an acidity of 18.8 in cases not showing casts.

From all this, the deduction which seems warranted is that the height of the urinary acidity does not determine the presence of albumin, blood cells and casts.

ALBUMINURIA. Seventy-seven per cent. of the entire series showed albuminuria as a result of the effort.

Out of 36 “baseball” cases, 26 showed albumin and 10 showed none.

Out of 18 “track” cases, 16 showed albumin and 2 showed none.

The inference here is plain that albuminuria occurs more frequently as a result of strenuous effort, *i. e.*, those cases in which there is the greatest amount of circulatory disturbance.

MICROSCOPIC FINDINGS. *Casts and Red Blood.* After running on the track 71 per cent. had hyaline and granular casts and a small percentage of red blood cells. After baseball 23 per cent. had hyaline and granular casts or red blood cells. From this we may also infer that the more strenuous type of exertion causes casts and blood cells to appear in the urine.

RÉSUMÉ. These observations show that in the most severe type of exertion (Marathon race), albumin and casts and red blood cells occur in all individuals. The casts were of the broad and narrow, hyaline and granular variety. Some of the casts showed red and white corpuscles. The amount of albumin was greatest in those who ran most strenuously, finishing earliest, 3 hours 14 minutes to 4 hours 15 minutes.

Observations of the blood-pressures and pulse-rate in these cases showed that the largest amount of albumin and blood and casts occurred in those individuals who showed the greatest degree of

circulatory disturbance. This was manifested by a marked fall in both the maximum blood-pressure and in the pulse-pressure.

In the less strenuous type of exertion we usually find an increased urinary acidity, albuminuria, cylindruria, and at times blood cells.

A critical analysis of these findings, however, shows, first of all, that in the more strenuous effort the amount of albumin, the presence of blood cells and the number and type of casts all depict a more serious renal disturbance than is found in the less strenuous form of exercise.

Urinary acidity was increased after exercise in 85 per cent. of the cases, but it did not occur more frequently, nor was the acidity higher in the severe exertion cases than in the milder ones.

There is a positive relationship between the degree of albuminuria and cylindruria and the type of physical exertion; but these observations show that no such relationship can be established between the urinary acidity and the occurrence of albumin, casts and blood cells in the urine.

THE ASSOCIATION OF FEVER WITH FRACTURE OF THE SKULL.

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A SLIGHT rise of temperature is so common after fracture of the skull—with and without injury of the intracranial contents—that one rather expects it in almost every case; the rise is rarely above 100° F., is short-lived and lasts for approximately twenty-four hours, after which subsidence to the normal occurs and the latter continues until convalescence is completed. In some of the patients, however, fever assumes a more important role: it rises to extraordinary heights; it persists for comparatively long periods of time; it indicates some grave complication or the reaction to an extensive trauma. The cases in this latter group form the basis for this communication.

Such fever occurred in 15 of a series of 72 cases of fracture of the skull which were recently studied—21 per cent. In another series of cases of fracture of the skull, admitted to the hospital in a different period of time, 22 patients of a total of 77 developed fever—29 per cent. In the 15 febrile cases of the first series the fractures were situated in the posterior fossa in 6, and in the middle fossa in 2; in the others the fractures were distributed over the vertex and sides of the skull. One fracture was compound externally; one communicated with the middle ear and 2 with the nasal cavities; the

others were all closed fractures. Eight of the patients who developed fever died; in 4 of these the cause of death was a meningitis.

The cases which developed fever can be divided into the following groups:

1. The Ordinary Cases:

In a number of the febrile cases the temperature was of a moderate degree and the cause for the latter could not be established. In one of the cases (No. 192204) fever was present for two days. Except for the fact that it persisted somewhat longer than usual it approximated to the initial reaction so frequently seen and would, ordinarily, draw no extra comment. In another patient (No. 156919) there was an initial rise of temperature which fell promptly as it usually does; on the fourth day it rose again to a moderate height to fall to the normal after twenty-four hours more. Both of these patients recovered and the cause of the temperature remains obscure.

Case No. 192204. A boy, aged seven years, fell from a fire-escape a distance of thirty feet and landed on the front and side of his head. For a period of thirty minutes he was unconscious; thereafter he vomited a number of times and complained of pain in the left side of his head. The physical examination showed a hematoma of the scalp and the roentgen ray showed a frontoparietal fracture. The neurological status was normal except for some hyperactivity of the knee-jerks. The character of the fever is indicated in Fig. 1. The patient made an uninterrupted recovery.

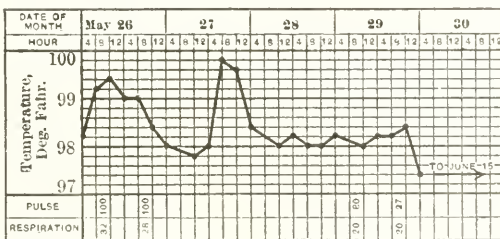


FIG. 1

Case No. 156919. A boy, aged seven years, fell a distance of eight feet and struck the right side of his head. He was unduly quiet thereafter and complained of a dull headache; he vomited after taking some food. There was a hematoma of the right parietal region and the roentgen ray demonstrated that the fracture lay directly underneath and extended into the mastoid. There were no neurological disturbances. The fever is shown in Fig. 2. An uninterrupted recovery followed.

2. The Fatal Cases:

In the following case an excessive degree of fever was associated with an extensive cranial fracture and with widespread disorganization of the intracranial contents. The notes of the case follow.

Case No. 179660. A six-year-old girl who was thrown from an automobile struck the pavement with the top and back of her

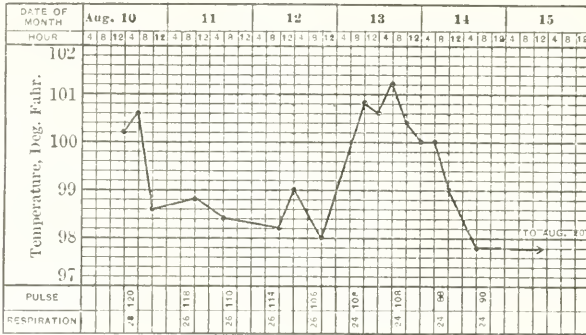


FIG. 2

head. There were several large hematomata over the occiput and vertex and behind the ear. The neurological disturbances which

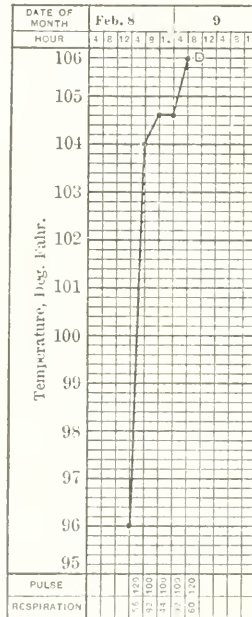


FIG. 3

pointed to a brain injury included (1) unequally dilated pupils, neither of which reacted; (2) internal rectus paralysis; (3) beginning

papilledema; (4) spasticity of all four extremities, with absent abdominal and exaggerated limb reflexes and elicitable abnormal reflexes, including Babinski, Gordon and Oppenheim responses; (5) peculiar athetoid movements of the hands, with flexion of the hands at the wrists; (6) stupor, with Cheyne-Stokes breathing. At the time of death—about twenty hours after the injury—there was (7) complete flaccidity, with (8) absent reflexes and (9) widely dilated pupils. Prior to death the temperature reached 106.8° F. (Fig. 3).

The cause of death in this child was evidently a widespread disorganization of brain substance, aided by a marked grade of intracranial compression from edema and hemorrhage. The temperature, owing to the shortness of time elapsing between the injury and death, assumes the characteristics of an antemortem rise. Our knowledge in this regard is, however, very deficient, and it is quite probable that this as well as other antemortem rises of temperature have something in common with disturbances of the heat-regulating centers.

The notes of two other fatal cases are given in which fever formed one of the prominent parts of the symptom-complex.

Case No. 190666. A fifty-five-year-old patient sustained a bad crushing fracture of the right malar region and side of the skull immediately opposed to it; there was very marked protrusion of the orbital contents. Besides the last the clinical picture included much shock; marked restlessness; fever (Fig. 4); a sluggish,

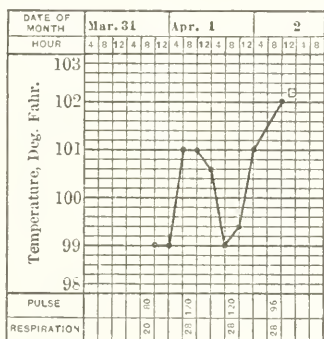


FIG. 4

irritable and disturbed mentality, which changed to stupor, deepened to coma, and terminated in death forty-eight hours after the injury was sustained. The character of the symptoms, taken in conjunction with the location of the fracture, pointed to disturbances in the frontal lobe.

Case No. 173080. In the second of these two patients, a woman, aged sixty years, a fracture of the base of the skull was associated,

clinically, with rigidity of the neck, coma, general spasticity and loss of control of the sphincters. Death occurred seventy-two hours after the injury. Fever (Fig. 5) was present during the entire period the patient was in the hospital.

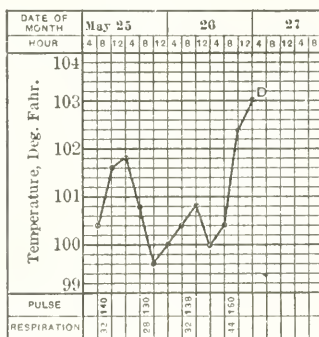


FIG. 5

In both of these patients the probabilities are very strong that there was considerable intracranial hemorrhage; in the second patient the symptoms indicated cerebral compression; in neither of them was there any indication present of any infectious process or of any complicating condition which could account for the irregular temperature.

3. Fever in Compound Fractures:

In one patient fever, as noted in Fig. 6 (Case No. 185032), was associated with a compound fracture. The scalp wound had been

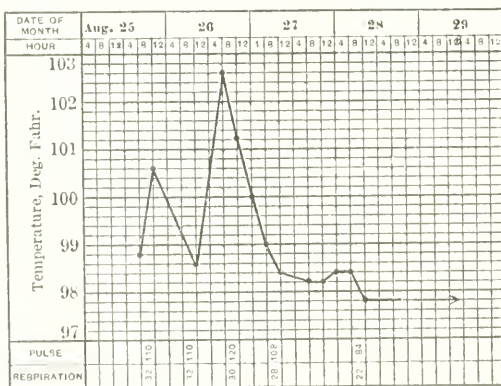


FIG. 6

sutured immediately and, apparently, had healed by primary intention. In the absence of any other cause it is quite likely, however, that infection was present in the wound and was combated

by the natural powers of the body without any disturbance of the healing.

A very remarkable case is the following:

Case No. 193199. The patient—a child, aged six years—sustained a fracture in the posterior fossa of the skull. Nothing extraordinary was noted at the time of admission to the hospital, and there were no signs of disturbed neurological function. Fever of a slight grade (Fig. 7) was present from the beginning, and by the fifth day it had risen to 102.4° F. During the course of the routine examination a laceration was discovered in one drum-head, and owing to the positive history of no preceding affection of the ear the otologist (Dr. Braun) rendered the opinion that the fracture had opened into the middle ear and, presumably, had become secondarily infected. The otitis subsided very quickly, however, and ten days after the injury the perforation in the drum-head had closed completely. On the thirteenth day the temperature reached 104° F. Lumbar puncture had hitherto not been practised, owing to the recent work of Weed and his co-workers, and of Wegeforth and Latham, but at this point it was done, and was subsequently repeated two days later; except for some increase of pressure on the first tapping the procedure yielded negative information both times: there were 3 cells per cubic millimeter and the fluid was bacteriologically sterile.

During the second week the following neurological signs developed rather slowly and irregularly: (1) A weakness of one facial nerve; (2) a convergent squint; (3) slight twitching of the left upper extremity; (4) very slight retraction of the head, with moderate rigidity of the neck which could, however, be forcibly overcome; (5) tendency to a Kernig on the right side; (6) irritability. No abnormality could be discovered in the chest or abdomen and no focus of infection could be demonstrated in any of the limbs. In the third week the temperature gradually subsided to normal, the signs and symptoms all gradually disappeared and thereafter the child made a perfect recovery.

The question in this particular case was whether the child had had a basilar meningitis, from which it had recovered, or whether the fever was due to some other cause. The probabilities of a meningitis were much strengthened by the fact that the patient was admitted into the hospital a short time after the termination of the influenza epidemic; coincident with the stay of this patient in the hospital another child had been admitted to the same ward and had gone through a similar clinical picture—in which similar negative laboratory findings were demonstrated—and, after it had died, an autopsy revealed a basilar meningitis, with a shaggy, greenish exudate in which influenza-like organisms were demonstrable in smears. The physical findings were in no way conclusive, inasmuch as cases of basilar or posterior fossa fractures quite

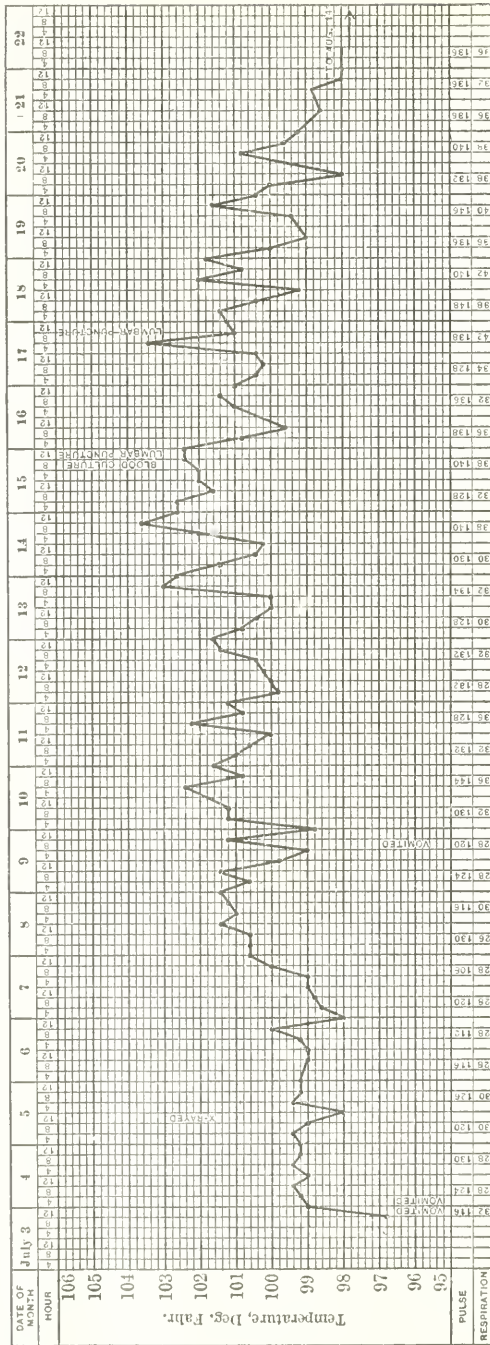


Fig. 7

commonly exhibit some of the signs of meningeal irritation. The probabilities, when all things are considered, seem to be that the physical findings were due to irritation of the meninges by the extravasation of blood and that the fever was due to absorption of the latter and to the aseptic inflammatory processes necessary to the proper repair of the fracture.

4. Fever Due to Complications:

Fever occurred also as a reflection of some complicating condition. The most prominent of these was a meningitis. The two cases given as examples show the varieties of fever which were present when this complication appeared after fracture of the skull; in the one (No. 177900) the infection was fulminant, the fever was high and the clinical course was very short and terminated in a fatality; in the other (No. 173371) the symptoms and fever made their appearance after several days and the course was more protracted.

Case No. 177900. The patient had a fracture in the frontal region and the roentgen ray showed, clearly, the communication with the frontonasal sinuses. The signs of meningitis were developed fully within twenty-four hours and the spinal fluid was loaded with polymorphonuclear cells and contained type I pneumococci. Fig. 8 shows the character of the fever.

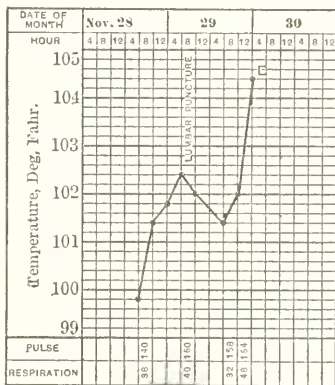


FIG. 8

Case No. 173371. In falling a five-year-old lad struck the pavement with the back of his head. He vomited and became unconscious; later this disappeared. The eyeballs showed some nystagmus when turned to the right, otherwise the neurological status was normal. Three days later the temperature rose to 105° F. The patient became apathetic; he assumed an attitude of complete flexion; there was moderate opisthotonos, a bilateral Kernig, and a suggestion of a Babinski. The spinal fluid contained many cells and Type IV pneumococci. The patient died.

The postmortem examination showed a fracture extending to the left jugular bulb and into the left middle ear and a general purulent meningitis.

Fig. 9 shows the temperature curve.

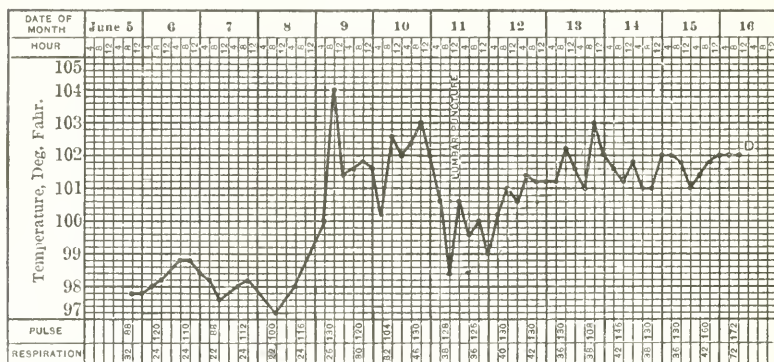


FIG. 9

5. Fever in the Operated Cases:

Fever in the operated cases was present in some both before and after operation and in others only after operation. In the latter it was frequently so because the patients were operated upon immediately after admission to the hospital and there was no opportunity allowed before the interference for the temperature to rise. When excessive fever developed after operation there was never any conclusive proof that it was directly due to the operative intervention, and, in all probability, the nature of the injury and of the resultant pathological changes contributed largely, if not entirely, to the pyrexia. The following cases are good examples of those in this group.

Case No. 161336. One hour before admission the patient fell down an elevator shaft. The patient was pale, semiconscious and in marked shock. In the parietotemporoöccipital region was a large hematoma. Blood was escaping from the ear. There was a progressive lowering of the pulse-rate to forty-four beats to the minute. The neurological status included (1) an initial period in which the reflexes were absent; (2) periods of excitation and stupor alternating with one another; (3) paralysis of left arm and leg; (4) reappearance of the reflexes which became hyperactive; (5) clonus at both ankles.

The operation, which was done four hours after the injury, showed a fracture extending from the occiput into the temporal bone and mastoid and which was depressed in areas. The dura was plum-colored and there was a perforation in the lateral sinus. An extensive subdural hemorrhage was also present and the brain

was badly lacerated. Bilateral subtemporal decompression was done.

On the following day improvement was present in that power began to return in the arm. Twenty-four hours later, however, the patient's condition became worse and death followed shortly. The character of the fever is shown in Fig. 10.

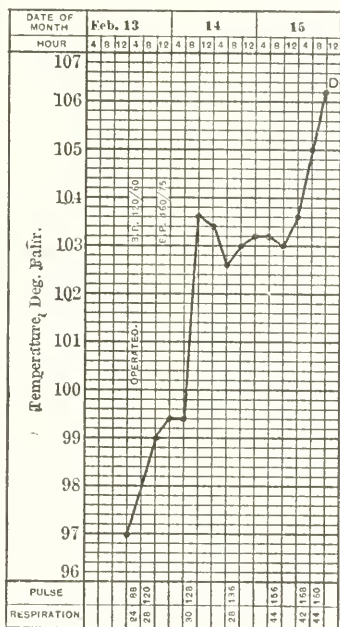


Fig. 10

Case No. 148405. A boy, aged nine years, was run over on the street and was brought immediately thereafter to the hospital. On admission the boy was in stupor and was bleeding from the nose and mouth. The neurological findings included (1) left facial weakness; (2) twitchings of left upper limb; (3) convulsions beginning in the left arm, spreading to the left leg and to the opposite side of the body. Within the next twenty-four hours the signs of compression grew more marked.

Operation¹ was done on the day following the injury. A flap operation was done. The exploration showed (1) that no hemorrhage was present; (2) great tension and edema of the brain; (3) some bloody serum in the basilar portion. No improvement followed the operation and the patient died approximately twenty-four hours later.

¹ The reasons for the operation and for the exploration through a bone flap are not apparent from the history.

In Case No. 148405 fever (Fig. 11) was present from the time of admission to the hospital and reached 102.8° F. within twelve hours. At the time of operation—forty-eight hours after the injury—the temperature had reached 106.6° F. There was marked hyperpyrexia at the time of death. The injury included a basilar fracture and much disorganization of brain tissue, as evidenced by the great tension and widespread edema of the cortex.

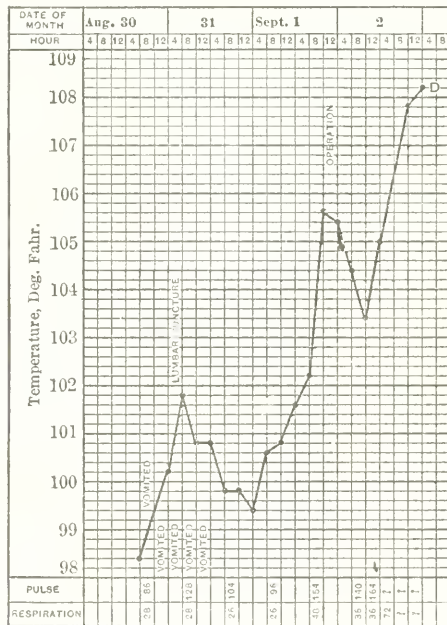


FIG. 11

Cases of operative infection are, of course, not included in this discussion.

6. Fever after Lumbar Puncture:

In one of the patients fever occurred after lumbar puncture. A child sustained a fracture in the parietal region. On admission the patient was drowsy but otherwise exhibited no definite symptoms of any focal lesion. Twenty-four hours later there were indefinite signs referred to the lower extremities: the left seemed to have impaired power and the right was somewhat spastic. Lumbar puncture was done at this point and some bloody fluid was released from the spinal canal. Up to this time the temperature had been normal, but immediately thereafter it began to rise and in an additional twenty-four hours it reached 101.4° F. Operation, which was done at this time, demonstrated extradural bleeding over an intact dura, and was followed, shortly, by a fatality (Fig. 12).

COMMENT. Fever associated with injury of the skull and of the intracranial contents occurs much more commonly than a perusal of the literature would lead one to believe; and while in the presence of some definite infection or other lesion the origin of the temperature is perfectly apparent, in others the cause for the fever is obscure and the mechanism for its appearance, especially when hyperpyrexia is present, is ordinarily said to involve disturbances of the heat-regulating centers.

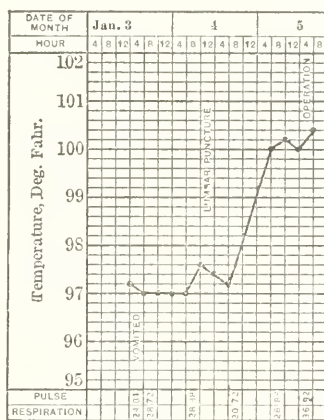


FIG. 12

It was most instructive to compare with these cranial and intracranial injuries a series of cases in which a fracture of the skull could be ruled out but in which the character of the symptoms and the physical findings indicated that a state of concussion (brain contusion) was present. It was cause for much surprise to learn that between 20 and 25 per cent. of the latter cases developed fever of one kind or another during their stay in the hospital. As a general rule the fever was of a very moderate kind and compared with the variety described in group 1. In a very small minority the temperature rose to greater heights. The following cases form excellent illustrations.

Case No. 181734. A young child was thrown in an automobile accident and was brought immediately to the hospital. Except for a small hematoma in the scalp nothing abnormal could be detected and within twenty-four hours the child was perfectly normal, with the exception of the low grade of fever noted in Fig. 13. No adequate cause for the temperature besides the trauma to the head could be discovered. The diagnosis was "concussion."

Case No. 186469. A man, aged forty-three years, was struck in the head by a moving car forty-eight hours before admission to the hospital. He has been in a very dazed condition since, has

complained of much headache and has vomited a number of times. A complete examination in the hospital showed a normal neurological status. With rest in bed the symptoms rapidly disappeared and forty-eight hours later when the man left the hospital no abnormality of any kind could be distinguished. There was absolutely no evidence of any skull fracture.

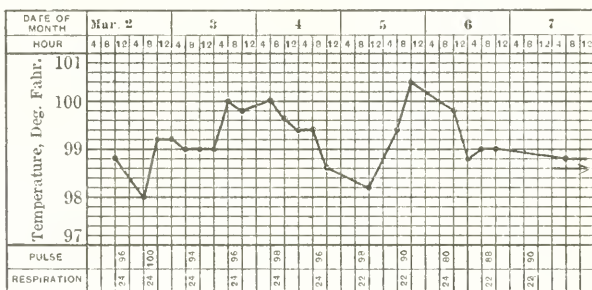


FIG. 13

The fever which this man developed in the hospital is extraordinary. Immediately on admission the temperature (Fig. 14) was 102° F.; within a few hours it rose to 104° F., and thereafter it gradually fell until the time of discharge from the hospital. No other cause beside the head trauma could be demonstrated which could adequately account for the fever. The final diagnosis was "concussion."

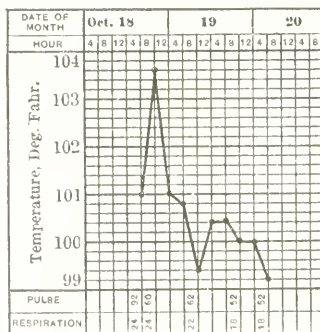


FIG. 14

When fever appears in the cases of this kind, as well as in those in which the brain contusion is associated with fracture of the skull, the assumption seems justified that the more or less widespread disorganization of brain tissue has, probably, primarily involved the heat-regulating centers, and that any fever which appears is due to

the latter disturbance. Implication of these centers could very possibly result secondarily from a general intracranial compression resulting from a sudden cerebral edema following the trauma or more slowly when the compression is due to other causes. Fever under these circumstances would be liable to be a hyperpyrexia. On the other hand there are cases with a more moderate or low grade of fever in which the symptoms and physical findings indicate a more restricted disorganization of brain tissue; possibly in these the temperature finds its origin in the inflammatory process (encephalitis?) essential to the proper repair of the injury.

It is quite possible that in some of the patients with fracture of the skull the phenomenon of fever is connected with the absorption of extravasated blood. In fractures of the long bones an extensive hematoma formation not infrequently is accompanied with a low grade of fever which persists for a short time.

In a series of 61 uncomplicated and closed fractures of the long bones fever was present in approximately one-third. The fever was of a very low grade, usually varied between 100° and 101° F., very rarely reached above 101° F., and never presented the bizarre forms described above with the cases of fracture of the skull or concussion of the brain.

Confirmation of this observation is found in the clinical courses of hematomata of the buttocks: quite commonly these are associated with an intermittent fever which is liable to continue to mount to 103° and 104° F. daily in the absence of any demonstrable infectious or suppurative process until the clot is totally absorbed. A drop of the temperature frequently follows the aspiration of the liquefied portions of the clot, and it is often necessary to incise freely into the hematoma before the temperature disappears; evidently the fluid carries with it some factor which serves to keep up the fever. It seems quite reasonable to assume that a similar mechanism is functioning in some of the cases of fever following a head injury, and the assumption seems especially applicable to the cases of basilar fracture, with hemorrhage into the middle and posterior fossae of the skull. In these patients lumbar puncture almost invariably releases a bloody fluid which is bacteriologically negative, and which, microscopically, shows very few cellular elements outside of the red blood cells; and the indicated findings serve to negative any impression of an infectious meningitis which might seem probable because of the exhibition of more or less marked symptoms of meningeal irritation. As anticipated in the notes of Case No. 193199—which seems to be an excellent example of this combination of circumstances—the probabilities are very strong that the fever owes its origin to the absorption of extravasated blood, and the physical findings indicate irritation of the meninges by the presence of a foreign fluid.

Our attention to the question of fever after cranial and intra-

cranial injuries was stimulated by some work of Weed and his co-workers. Briefly stated their work consisted of the production of an artificial bacteremia, after which cerebrospinal fluid was released by lumbar puncture; the procedure was followed by a cerebrospinal meningitis. Confirmation of this experimental work in clinical medicine was recently reported by Wegeforth and Latham, who found in a number of general and pulmonary pneumococcus infections that the release of normal cerebrospinal fluid by lumbar puncture was followed by meningeal infection; they describe five cases of their own and refer to others in the literature. Our Case No. 188349 seems to belong somewhere in this group; in this patient a lumbar puncture, with the release of some bloody fluid, practised approximately twenty-four hours after a cranial and intracranial injury, was followed by a rise of temperature. Apparently this seems to be a mild case of infection which, perhaps, under another subsequent course of events might have spontaneously disappeared. The source from which the infection took its origin could very possibly be a dormant one and lie hidden in the tonsils, the teeth or other similar locality. The absence of any true purulent meningitis would seem to indicate that mild cases of infection can occur from which retrogression can be spontaneous. Since the appearance of the communication of Weed we have been very careful and very backward about doing lumbar puncture after cranial and intracranial injury.

In considering the mechanism of fracture of the skull, with intracranial injury, attention was attracted to the fact that a release of cerebrospinal fluid must also occur into the adjacent tissues when a communication is established by dural laceration with the subarachnoid space. An analogous situation is established to the release of cerebrospinal fluid by lumbar puncture; and it is not unreasonable to assume, further, that in the presence of some hidden or dormant focus of infection in the body, either nearby or at a distance, fever would follow. The assumption offers a very satisfactory explanation for the initial rises of temperature which are commonly found after fractures of the skull; it offers an equally plausible explanation for the sudden and sharp rises of temperature which are sometimes seen to follow decompression or other cranial operations in which the dura is opened and cerebrospinal fluid is released from the subarachnoid space. The fact that the process does not terminate always in a suppurative stage should not appear extraordinary, and the retrogression is probably due to the fact that the organism is possibly accustomed to the variety of infection which is lighted up or that the body's natural resistance powers are amply sufficient to quickly bring the process under control. In any case the insult of lumbar puncture, trauma or operative interference, with a subsequent release of cerebrospinal fluid, seems to create a *locus minoris resistentia* and the injured area forms a

fixation-point for any pathogenic organisms which, at the moment, are circulating in the blood-stream.

It seems very probable, when all things are considered, that in any particular case more than one of the factors indicated in this communication may be operative to account for any fever which develops. Only in a comparatively few cases is it possible for one to put one's finger accurately upon the actual mechanism.

SUBCUTANEOUS EMPHYSEMA: A COMPLICATION OF INFLUENZA PNEUMONIA. REPORT OF SEVEN CASES.

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RECENT clinical reports have mentioned subcutaneous emphysema as a rare complication of influenzal bronchopneumonia. Thus, Symmers¹ records 3 cases; Berkley and Coffen² 11; Clark and Synnott³ 12; Blanton and Irons⁴ and Stone and Swift⁵ merely mention its occurrence. Leichtenstern,⁶ in his exhaustive monograph on influenza, makes no note of this complication. Our own experience comprises a total of 9 cases, of which we have studied 7 cases carefully, and these are herewith presented. In about 3000 cases of influenzal pneumonia subcutaneous emphysema occurred in 0.3 per cent., and in the entire series of over 12,000 cases of influenza in only 0.07 per cent.

CLINICAL FEATURES OF INFLUENZA PNEUMONIA. The clinical picture of influenza pneumonia has been so often described that we do not deem it necessary to repeat it here. Our experiences, on the whole, correspond to all previous reports. We desire to emphasize, however, certain features of the disease, not only because they were apparently characteristic of the picture but because they may be significant factors in the production of emphysema.

1. *Toxemia.* This was striking early in the epidemic and entirely out of proportion to all physical findings.

¹ Jour. Am. Med. Assn., 1918, lxxi, 1482.

² Ibid., 1919, lxxii, 535.

³ AM. JOUR. MED. SC., 1919, clvii, 219.

⁴ Jour. Am. Med. Assn., 1918, lxxi, 1988.

⁵ Ibid., 1919, lxxii, 487.

⁶ Influenza, 1912. Alfred Hölder, Wien u. Leipzig.

2. *The Paroxysmal Cough.* This occurred early, was particularly distressing and closely resembled the cough of pertussis, excepting the absence of the "whoop" at the end of the paroxysms.

3. *Epistaxis and General Tendency to Hemorrhage.*

4. *The Frequency of Pain in the Chest.* The rapidity with which this developed was particularly noticeable, physical examination failing to reveal any cause.

5. *Cyanosis and Dyspnea.* The purple hue of the face, upper chest, and finger nails, at once suggested cardiac failure, but on physical examination, heart tones were generally good and there was usually no evidence of right heart failure. Blood-pressures were practically normal.

6. *The Relative Paucity of Physical Findings and the Rapidity with which the Signs of Consolidation Developed.* It is noteworthy that on admission a few crepitant rales were heard posteriorly. Percussion revealed a distinctly hyperresonant note, and this had no apparent relation to the amount of consolidation.

REPORT OF CASES.

CASE I.—Lieut. P. Taken ill and admitted October 2, 1919, with headache, sore-throat and general aching. Physical examination revealed a young, fairly well-nourished man, face congested, pulse of fair quality, temperature 103°, respirations 24. Many crepitant rales in right lower lobe; impaired resonance and diminished breath sounds.

October 4. Dulness over the right lower lobe; bronchovesicular breathing. The roentgen-ray report showed spot shadows in the lower right.

October 9. Slight cyanosis of nose, lips and ears and the physical signs of consolidation in right lower lobe. On the left side many crepitant rales. At 2 P.M. examination of the chest revealed loud crackling sounds over the apices. On palpation of these areas a fine crepitation was obtained and a diagnosis of subcutaneous emphysema made. The extent of the involvement at this time was the left supraclavicular space and upper part of the left chest. The patient had no complaint of precordial or pleuritic pain at this time. On repeated questioning he could not associate his swelling in the neck with any cough; the patient was unaware of it until it was mentioned to him by the physician. The temperature showed no alteration from that on the previous day. The respirations were not changed in rate or excursion. The roentgen-ray report on this date revealed a shadow in the right lower lobe; no evidence of pneumothorax.

October 10. The air extended bilaterally and involved the chest, neck and upper part of the abdominal wall, interfering with examination of the chest.

October 13. The emphysema now involved the left side of the face. The left eye was closed because of emphysema of the lids.



FIG. 1.—Note emphysema of left eyelid.

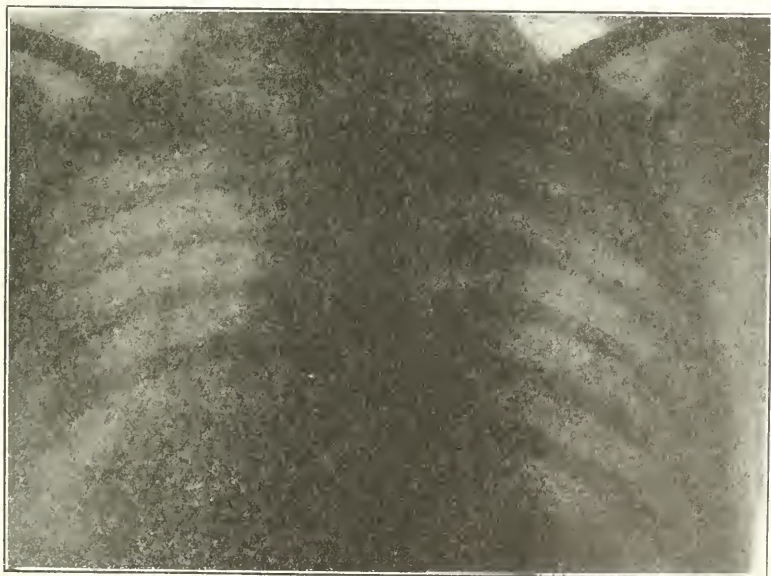


FIG. 2.—Note emphysema of supraclavicular tissues.

(Fig. 1). The upper and lower extremities were also involved. The scrotum was distended to about one and one-half times its normal size. The patient had the appearance of a nephritic.

Roentgen-ray Reports. October 14. Extensive quantities of "gas" shown in tissues of chest, neck (Fig. 2), arms down to wrist,

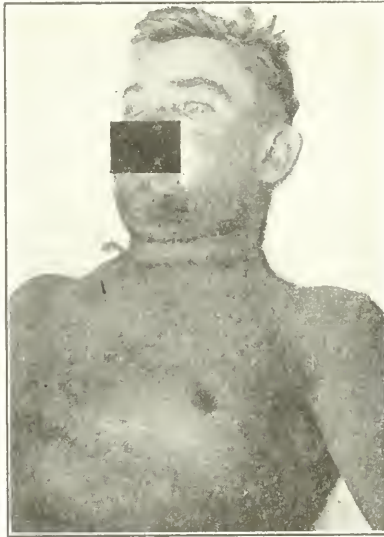


FIG. 3.—Note emphysema of neck and upper chest.



FIG. 4.—Note emphysema of neck.

over abdominal muscles and through the pelvis, scrotum and legs (Fig. 6).

October 17. Spot shadows throughout both lungs. Dilated heart. "Gas" in quantities throughout trunk, pelvis, legs and arms and wrists.

October 19. "Gas" in the legs has diminished; chest and abdomen remained the same.



FIG. 5.—Acute ulcerative bronchiectasis; note the apparent necrotic condition of the walls.

October 14. Pneumococcus Type I reported in the blood and patient was given 100 c.c. antipneumococcus serum; this was repeated on the next day.

October 16. Patient complained of pain in the right side.

October 17. Fifty cubic centimeters of antipneumococcus serum. No difficulty in locating veins for intravenous injection and no apparent increase in the emphysema after the severe chill following the initial injection of serum. Patient showed no improvement in

general condition, but emphysema diminished, particularly about the face.

October 20. Patient died.

Blood culture: Pneumococcus Type 1. Leukocytes: October 3, 4000; October 10, 3400; October 15, 10,000. Anaërobic and aërobic cultures of "gas."

The skin was punctured under aseptic precaution and sterile salt solution introduced by capillary pipette. The washings were then cultured. Negative results after seven days' incubation at 37° C.

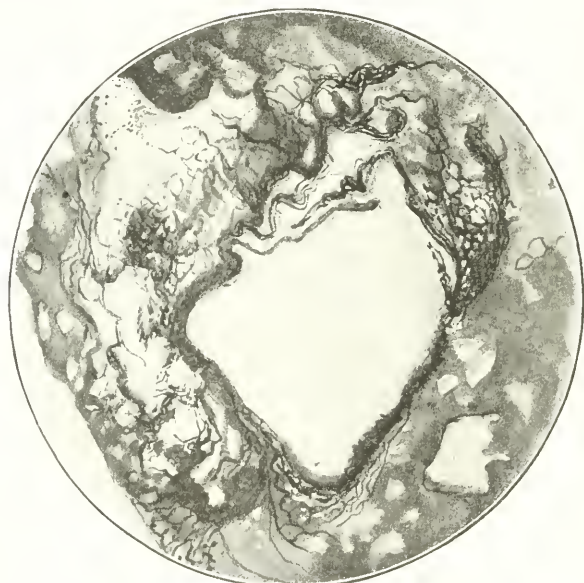


FIG. 6.—Ulcerative bronchitis; infiltration with air of peribronchial tissues. Note the torn, necrotic condition of the bronchial wall and the distention of the peribronchial areolar tissues.

Necropsy (18-196). Subcutaneous emphysema; left eyelids, left temporal region, cheeks and entire neck, entire chest and abdomen to anterior scapular line without involving gluteal region, left side of scrotum, left lower extremity to knee, right lower extremity to thigh. Subfascial and fascial emphysema of neck, axilla, chest and abdomen. Slight icterus. Emphysema of mediastinum. Edema of areolar tissue of mediastinum. Acute fibrinous pleuritis, right. Early lobular bronchopneumonia in left upper lobe. Confluent bronchopneumonia in left lower lobe. Compensatory inflation on anterior edge of entire lung, left. Bronchopneumonia, upper and lower lobe; compensatory inflation, anterior edge, right lung. Purulent bronchitis with acute ulcerative bronchiectasis, more marked in left lung. Acute fibrinopurulent bronchitis. Cloudy

swelling and slight right-sided dilatation of heart. Acute follicular splenitis. Congestion and edema of adrenals. Acute parenchymatous nephritis. Cloudy swelling and terminal congestion of liver. Cloudy swelling and congestion of the pancreas. Lymphoid hyperplasia and congestion of intestines. Edema of pia-arachnoid; congestion of brain.

Microscopic Findings: Lung: fibrinopurulent bronchopneumonia; areas of hemorrhage; marked edema; acute ulcerative bronchiectasis; dilatation of peribronchial spaces; areas of necrosis; acute emphysema. Heart: congestion; cloudy swelling; conglutination and hyaline thrombi; acute fibrinous pericarditis. Spleen: acute diffuse splenitis; massive hemorrhages; partial necrosis of reticulum. Adrenal: lipoid exhaustion; congestion. Kidneys: acute glomerulotubular nephritis. Liver: congestion; cloudy swelling; focal toxic necrosis. Brain: cloudy swelling of ganglion cells; congestion.

CASE II.—Private M. Admitted February 18, 1919. Previous history: measles, pertussis, scarlet fever. Onset: two days before admission he complained of cough, chilly sensation, fever. On admission: a young, well-nourished man, apparently not very sick, complaining of headache, pain in the extremities and cough. Examination: no definite lung finding. A diagnosis of influenza was then made on the basis of general appearance. Patient showed no change until three days later, when many rales were noted throughout the chest.

February 22. Left lower dulness, distant bronchial breathing and fine crepitant rales; right lower dulness and rales.

February 24. Complained of intense pain in the right chest. Examination showed dulness, bronchial breathing, rales; no evidence of friction rub. On the left side the physical findings were unchanged, but notation was made of diminished breath sounds on left side.

February 25. Condition poor, pulse could not be obtained, cyanosis intense; hyperresonance over left chest anteriorly; in the left midaxillary line: dulness, breath sounds present. The heart borders could not be outlined on percussion; no visible apex impulse. On auscultation over the pulmonic area a loud crackling sound was heard as the stethoscope was placed on the skin. On palpating this area was distinct; fine crepitations in the subcutaneous tissue were obtained. This area extended from the second intercostal space to the nipple proper. The breath sounds were diminished; the heart tones were not audible. The clinical picture at once suggested a pneumothorax with subcutaneous emphysema. 4 P.M.: The emphysema had spread to the clavicle on the left side and could be felt over the sternum. It also extended to a slight degree below the left nipple at 6 P.M.: subcutaneous emphysema had extended laterally on the left side and reached the midaxillary line. The

patient was very cyanotic. The upper extremities were cold and covered with a clammy perspiration. Patient complained of pain and numbness of feet; this complaint commenced at 12 P.M. The feet were cold; there was no pulsation in the dorsalis pedis artery, but the femoral pulse and sounds could be obtained. The abdomen was tender and slightly distended. 7 P.M.: emphysema had not spread; pulse could not be obtained. 8 P.M.: patient died.

Roentgen-ray Reports. 1. Spot shadow, right lower, February 18. 2. "Gas" in the subcutaneous tissue of left chest. No evidence of pneumothorax.

Laboratory Reports. Sputum: Streptococcus hemolyticus. Blood Culture: Negative. Leukocytes: February 24, 6900.

Necropsy (19-364). Subcutaneous emphysema of neck, left upper chest, upper part of left abdomen. Emphysema of anterior mediastinum. Left pneumothorax. Zenker's hyaline degeneration of abdominal muscles. Bilateral acute fibrinous pleuritis. Confluent bronchopneumonia of left basal lobe. Patchy bronchopneumonia of left upper lobe. Inflation of lung borders. Confluent bronchopneumonia of right upper and lower lobes; inflation of borders. Purulent bronchitis. Cloudy swelling and dilatation of right heart. Acute follicular splenitis. Congestion of adrenals. Congestion of kidneys; acute parenchymatous nephritis. Acute tonsillitis. Cloudy swelling of liver. Cloudy swelling of pancreas. Slight congestion of intestines. Slight congestion and edema of pia-arachnoid. Petechial hemorrhages of brain.

Microscopic Examination. Lung: fibrinocatarrhal bronchopneumonia. Ulcerative bronchitis. Marked congestion. Heart: slight congestion; cloudy swelling. Spleen: acute follicular splenitis. Adrenal: lipoid exhaustion; edema; congestion. Kidneys; extreme congestion; acute tubular nephritis. Liver: cloudy swelling; biliary pigmentation. Brain: focal hemorrhage; cloudy swelling of ganglion cells.

CASE III.—Private B. Admitted October 3, complaining of sore-throat.

October 9. Many rales left base posteriorly; temperature, 104.4; pulse, 112; respiration, 48.

October 13. Patient was reported as a case of subcutaneous emphysema and notations on the brief showed it had developed on the left side, upper part of the chest, on the evening of October 13.

October 14. Examination showed a very robust young man, cyanotic and dyspneic, very uncomfortable and toxic. The emphysema involved the face on both sides and the patient had the appearance of a case of mumps; palpation revealed definite crepitation. The eyelids were not involved except the right, which was but slightly swollen. Both sides of the neck were distended (Fig. 43). "Gas" was also present in the subcutaneous tissue of the chest anteriorly and posteriorly. The abdomen, anteriorly, appeared

distended; the skin was "ballooned" up from the underlying tissues as if a layer of air were interposed; on deep palpation crepitation was obtained. Both upper and lower extremities were involved; the scrotum was distended. There was no change in the clinical picture until October 17, when the patient began to complain of pain in the region of the larynx. Laryngoscopic examination on October 18 showed congestion of larynx, with some purulent secretion; cords normal.

October 19 to 24. The emphysema gradually diminished and the patient appeared to be improving.

October 25. Complained of pain on swallowing and dyspnea.

October 26. Exploratory aspiration of the right chest; needle used for local anesthesia was used as aspirator, no fluid but air returned. A larger needle was introduced and returned a large amount of air without blood or fluid. Comfortable during and immediately after aspiration. Thirty minutes later intense dyspnea, rapid pulse, dilated pupil.

October 27 and 28. Emphysema diminishing, condition poor; influenza immune serum intravenously.

October 29. Patient died.

Roentgen-ray Reports. October 14. Roentgen ray; extensive quantities of air throughout subcutaneous tissues of neck and chest, apparently following fascial planes over the abdomen, pelvis and gluteal region, right arm to elbow and left arm to elbow, left leg below knee and right leg below knee. Extensive spot shadow throughout lungs.

October 16. Gas showed more extensively throughout body (Fig. 4), more particularly in arms and legs.

October 17. Spot shadows throughout both lungs. Dilated left heart. Gas over the trunk, and arms to wrist, and legs half-way below knee.

October 18. The gas throughout tissues over trunk somewhat less prominent, but well marked in right arm.

October 19. Extension of gas in right hand. Chest and abdominal condition improved.

October 21. Gas in tissues over chest, neck, abdomen, thighs and arms appeared to be less than on previous day.

Laboratory Reports. White counts: October 16, 16,200; October 18, 17,500; October 25, 13,900. Sputum: Non-hemolytic streptococcus; staphylococcus; pneumococcus (type not determined). Urine: Many hyaline and granular casts. Specific gravity, 1028.

October 14. All cultures, aerobic and anaerobic, negative.

Necropsy (18-216). Subcutaneous emphysema of entire chest and abdomen. Prelaryngeal abscess. Acute bilateral fibrinous pleuritis. Confluent bronchopneumonia of both lungs. Compensatory inflation of anterior edges of both lungs. Acute purulent bronchitis and bronchiectasis. Acute diffuse splenitis. Cloudy

swelling and congestion of kidneys. Cloudy swelling and terminal congestion of liver. Acute adenitis of mesenteric lymph nodes. Acute myositis and hyaline degeneration in rectus muscles. Slight edema of pia-arachnoid.

Microscopic Examination. Lungs: Fibrinocatarrhal bronchopneumonia; ulcerative bronchitis; areas of hemorrhages; acute emphysema. Heart: congestion and cloudy swelling. Peribronchial lymph nodes: marked congestion; edema; sinus catarrh. Adrenal: lipoid exhaustion; congestion and edema; hyaline thrombosis. Kidneys: congestion; cloudy swelling. Liver: hydrops; congestion; hyaline thrombosis; slight biliary pigmentation.

CASE IV.—Private P. Admitted October 10, 1918. Previous history negative. Was sick three or four days before admission to hospital, complaining of severe backache, pain in the chest, vomiting, slight coryza; throat injected, a few scattered rales in both bases. The patient showed no clinical change until ten days later, when he developed a rigid neck and positive Kernig's sign. A spinal puncture was performed but proved to be negative, microscopically and bacteriologically.

October 21. Patient had marked difficulty in breathing and swallowing; examination revealed an acute laryngitis, acute inflammatory edema of the glottis, epiglottic folds and arytenoids. Aryepiglottic folds and arytenoids were markedly congested, interfering with respiration. High tracheotomy was performed under local anesthesia.

October 24. One of us was called in to see the case at this time and distinct crepitation was present in the tissue of supraclavicular spaces and neck. On observation during the day it was noted that the gas remained localized in neck region but increased in quantity.

October 25. Patient died.

Roentgen-ray Reports. October 12. Spot shadows in both lower lobes. Throat culture: Staphylococcus predominating. Leukocytes: October 12, 5800. Sputum: Staphylococcus; pneumococcus.

Necropsy (18-209). Subcutaneous emphysema of anterior neck. Operative wound of neck (tracheotomy). Cervical abscess. Bilateral fibrinopurulent pleuritis. Bilateral lobular bronchopneumonia of all lobes. Acute diffuse splenitis. Massive hemorrhage of right adrenal. Acute parenchymatous nephritis; congestion of kidney. Cloudy swelling of liver. Congestion and edema of pia-arachnoid. Lymphoid hyperplasia of intestines. Acute suppurative otitis media, right. Acute mastoiditis.

Microscopic Examination. Lungs: acute fibrinocatarrhal bronchopneumonia; edema; marked congestion; ulcerative bronchitis; acute inflation. Heart: congestion; cloudy swelling; peribronchial lymph nodes: congestion and edema; sinus catarrh. Spleen: acute diffuse splenitis. Adrenal: lipoid exhaustion; congestion. Liver: congestion; cloudy swelling. Kidneys: acute glomerulotubular

nephritis. Brain: cloudy swelling of ganglion cells; congestion; minute hemorrhages.

CASE V.—Lieut. S. Admitted to Base Hospital October 3, 1918. Previous history negative.

October 1. Onset, with general malaise and chilliness. On admission a robust young man, rather dyspneic, coughed persistently. Intense cyanosis of face; dulness of right lower lobe; bronchial breathing.

October 7. Extensive involvement of right lower and middle lobes, with dulness, bronchial breathing, crepitant and subcrepitant rales. Many small areas of dulness with many rales in the left side. Cyanosis and dyspnea very pronounced.

October 10. Distant crepitation over the entire right side of the chest and neck. The face was not involved.

October 11. Patient died.

Roentgen-ray Reports. October 8, 1918: shadows involving both lower lobes. Sputum bacteriology: streptococcus, pneumococcus, staphylococcus, *M. catarrhalis*.

Leukocytes: October 8, 1918, 6500.

CASE VI.—Private G. Admitted October 3, 1918. Previous history: exanthemata, including smallpox, when a child; fracture of ribs several years ago. Onset sudden, cough, pain in chest and fever. On admission: a robust young man, appearing not very sick, with cyanosis of face; throat purple and injected; no definite evidence of consolidation, many rales. Diagnosed severe influenza.

October 5. Consolidation lower left.

October 8. Subcutaneous emphysema in upper part of chest, neck, face. Patient delirious; petechial eruption on skin.

October 9 to 12. No change; clear mentally.

October 18. Emphysema of subcutaneous tissue diminished; absent on chest.

October 21. Lungs clear; breath sounds high pitched; no rales.

November 1. Discharged from hospital as recovered.

Roentgen-ray Reports. October 14. Extensive quantities of gas in the tissues over neck, shoulders, abdominal muscles. Spot shadows throughout right lung. Shadow in lower left. Gas over gluteal region, thigh, legs and forearms.

October 16. Gas more extensive than on previous report.

October 18. Gas less marked in tissue than on previous report. Leukocytes: 7500.

CASE VII.—Private R. Admitted October 3, 1918, with diagnosis of influenza.

October 9. Many rales over right lower lung.

October 14. Developed bilateral lobular pneumonia.

October 15. Patient very weak, coughed persistently, sputum bloody.

October 16. Cyanosis of face. Mental condition sluggish.

October 18. Patient appeared very toxic and was delirious. Spinal puncture performed and 20 c.c. of clear fluid removed; this showed no increase in cells and no bacteria; globulin negative.

October 20. Condition serious; patient dyspneic and cyanotic. Subcutaneous emphysema developed, involving the face, neck, chest and upper and lower extremities bilaterally.

October 21. Patient's condition serious. The emphysema in the lower extremities diminished.

October 22. Subcutaneous emphysema had extended to waist line. Lower extremities free.

October 23. Subcutaneous emphysema increasing.

October 25. Intravenous injection of immune serum.

October 26. Weak; complains of pain in chest.

October 29. Emphysema disappearing. Gradual improvement. Discharged from hospital November 22, 1918, as cured.

Roentgen-ray Reports. October 15. Shadow in lower right.

October 20. Extensive spot shadows in lower right with same on left. Gas showing throughout muscles of trunk with some in the thighs, also in forearms.

October 21. Gas in tissues of neck, chest, abdomen and arms.

October 23. Gas extending.

In addition to the above one of us has observed a similar condition complicating measles. The emphysema was localized in the chest wall; the patient recovered. In another instance generalized subcutaneous emphysema developed postoperatively in a patient who had a pyopneumothorax. In this case the emphysema developed one day after operation; the patient was aspirated repeatedly prior to operation but never presented evidence of subcutaneous emphysema. When the emphysema did develop it was rapid and generalized, involving face, neck, chest, abdomen and extremities. This patient died.

CLINICAL ANALYSIS. An analysis of these cases from the clinical aspect reveals certain constant features.

The onset of the subcutaneous emphysema was apparently sudden, but after its appearance the "gas" spread relatively slowly, attaining its greatest extent in twenty-four to forty-eight hours.

The time of appearance of the emphysema, relative to the stage of influenza pneumonia, was not definite, but it is safe to say that in the majority of the cases the "gas" developed when the pneumonic process was well advanced. Table I shows this relationship.

TABLE I.—TIME OF DEVELOPMENT OF EMPHYSEMA.

Case No.	Influenza.	Pneumonia.	Emphysema.	Death or recovery.
I . .	October 2	October 9	October 9	October 19
II . .	February 18	February 22	February 25	February 25
III . .	October 3	October 5 or 9	October 14	October 29
IV . .	October 10	October 10	October 24	October 25
V . .	October 3	October 5 or 7	October 10	October 11
VI . .	October 3	October 5	October 8	Recovered.
VII . .	October 3	October 14	October 20	Recovered.

It is noteworthy that the paroxysmal cough, to which has been ascribed an important place in the possible etiology of the subcutaneous emphysema, occurs very early in the picture of influenza pneumonia, and that when the pneumonic process is well established cough is not common. It might be assumed that with a generalized pulmonary emphysema, or with a destructive softening of the lung parenchyma (Torrey and Grosh⁷) and an associated severe cough, rupture of alveoli could easily occur and be the source of emphysema. The striking contrast, however, of the late appearance of the emphysema and the absence of cough during that period suggest that the cough probably plays a minor role.

Symptoms associated with the development of the subcutaneous emphysema were, according to our experience, practically negative. The patient was generally unaware of the complication until it was pointed out to him. The temperature, pulse and respiration showed no change. Torrey and Grosh,⁷ however, state that "when in apparently respiratory extremis a patient would complain of pains, substernal and in the jugular fossæ, and crepitation would be noted in the subcutaneous tissues at the root of the neck, an immediate marked subjective relief was apparent, rapidly followed by a noticeable improvement in the respiratory excursion of the chest and the most striking decrease in cyanosis and jugular distention." Measurements of the respiratory excursion showing "that there was apparent an increase in the chest circumference during the illness and an abnormally small respiratory excursion, with a striking increase immediately as the subcutaneous emphysema gave vent to the air contained in the mediastinum."

We observed precordial pain in but one case, but pleuritic pain was common. Cyanosis was not relieved to any marked degree nor was the respiratory rate diminished as shown by our clinical record. Table II shows that the temperature, pulse and respiratory rate, before and after the appearance of the subcutaneous emphysema, were practically unchanged.

LOCATION OF SUBCUTANEOUS EMPHYSEMA. The subcutaneous emphysema has developed most frequently in the neck region. In one case it was first noticed in the region of the second left intercostal space. The supraclavicular spaces, neck, chest, face, extremities, abdomen and scrotum, have been involved. It is easily diagnosed by obtaining a fine crepitation on palpation, and on auscultation the stethoscope produces a loud crackling sound as it comes in contact with the skin.

ABSENCE OF SIGNS OF INFLAMMATION. There is no apparent change in the leukocytes with the development of the emphysema. Likewise there is no local skin eruption or inflammation. The physical condition seems but slightly affected by the development

⁷ AM. JOUR. MED. SC., 1919, clvii, 170.

TABLE II.—TEMPERATURE, PULSE, AND RESPIRATION BEFORE AND AFTER APPEARANCE OF EMPHYSEMA.

Date.	Before emphysema developed.			Date.	After emphysema developed.		
	Temp.	Pulse.	Resp.		Temp.	Pulse.	Resp.
CASE I:							
Oct. 7	105.0	112	28	Oct. 9	103.0	110	26
	100.0	92	26		101.0	90	30
Oct. 8	104.0	116	24	Oct. 10	101.8	84	24
	101.4	100	26		101.8	100	26
Feb. 22	100.0	92	22	Oct. 15	101.8	110	30
	102.2	92	22		100.2	84	40
CASE II:							
Feb. 23	102.8	90	24	Feb. 25	103.2	120?	36
	102.0	110	28		104.0	120?	36
	102.6	108	24		100.0	?	40
	102.6	92	24		102.0	?	48
Feb. 24	103.0	112	26				
	103.6	90	24				
	104.0	108	46				
	104.4	136	42				
	103.8	120	36				
102.0	120	36					
CASE III:							
Oct. 10	104.4	102	48	Oct. 13	100.0	116	44
Oct. 11	103.6	104	48		101.0	118	40
	103.8	112	36	Oct. 14	98.0	70	26
Oct. 12	101.0	98	36		100.0	110	30
	101.6	140	40	Oct. 15	100.0	100	22
					100.0	100	22
				Oct. 16	101.0	120	28
				Oct. 17	98.0	118	36
					101.0	120	30
CASE V.							
Oct. 8	103.0	98	36	Oct. 10	103.0	122	54
	102.0	140	38		102.0	120	56
	104.0	120	28				
Oct. 9	103.6	120	46				
	103.0	140	60				
CASE VI:							
Oct. 7	101.0	126	30	Oct. 8	101.0	96	30
	102.0	100	46		102.0	120	32
				Oct. 9	100.0	98	42
					102.6	120	42
				Oct. 10	101.2	96	30
CASE VII:							
Oct. 18	99.2	106	36	Oct. 20	103.2	144	48
	99.8	100	32		102.2	120	32
	101.2	110	44		Oct. 21	100.4	130
Oct. 19	99.0	120	46		102.4	128	52
	99.4	120	52		102.2	120	54
	98.8	140	52		102.8	120	14
	100.0	126	40	Oct. 22	101.0	104	14
					101.0	124	56
				101.2	112	50	
				101.2	122	54	

of even most extensive emphysema. In all of the patients the emphysema subsided considerably as the disease progressed and death was always due to associated conditions. Two of the cases recovered entirely.

Of the cases which developed subcutaneous emphysema it is noteworthy that in addition to the severity of the picture of pneumonia there were additional complications. Thus delirium occurred in one patient, meningismus in another and possibly a slight pneumothorax in still another. Prelaryngeal abscess and edema of the glottis were also encountered. The association of subcutaneous emphysema following tracheotomy has been reported previously,⁸ but not in association with pneumonia. In Case IV the occurrence of an emphysema following tracheotomy is noteworthy, since wounds of the larynx and trachea⁹ have been given as a cause of emphysema, but it seems evident that the emphysema in Case IV was not due to the laryngeal pathology.

In attempting to elicit a possible etiological factor in these cases we questioned our patients as to trauma and previous history of gas attacks. In none of these was any such history obtained.

The occurrence of only one case of pneumothorax diagnosed clinically and the constant absence of any evidence of pneumothorax on roentgen-ray examination in all our cases of subcutaneous emphysema is emphasized.

TREATMENT. The treatment in general was directed to the pneumonia or the associated complication rather than to the emphysema. As has been stated the development of the subcutaneous emphysema was not accompanied by any symptoms. The emphysema apparently will diminish or disappear without any operative or medicinal interference.

DISCUSSION OF ANATOMICAL FINDINGS. The subcutaneous emphysema in two of the cases was considerably more marked on the left than on the right side. The significance of this will be commented on later. The external appearance of the bodies has been described in the clinical part of this paper, and it need only be added that two of the patients presented the extreme lividity of the face and the body so frequently seen in fatal influenza.

The subcutaneous tissues when incised were moderately moist and slightly bloody, and, in a general way, had the appearance of innumerable small air bubbles in the alveolar tissue. Over the chest this distended areolar tissue measured about 15 mm. in its thickest part, over the abdomen about 5 mm. Sections from this tissue presented none of the changes associated with inflammation. Coagulation necrosis of the rectus muscles was met with in two cases;

⁸ Ashley and Wright: *Diseases of Children*, American edition, 1893. Quoted by Alexander, M. E., and Follett, E. C.: *Jour. Am. Med. Assn.*, 1919, lxxii, 930.

⁹ Lexer, E.: *General Surgery*. Quoted by Alexander, M. E., and Follett, E. C.: *Jour. Am. Med. Assn.*, 1919, lxxii, 930.

this condition was also present in non-emphysematous influenzal patients.

The mediastinum in two of the bodies resembled the subcutaneous tissues in general appearance. In two other bodies no changes were noted. In the first patient the areolar tissue throughout the mediastinum was edematous as well as emphysematous, forming a large mass over the pericardium, which, when dissected out, was found to weigh 165 grams. Otherwise the gross and minute anatomical changes in the various organs were similar to those in other influenza cases, and since a study of this disease has been published by one of us,¹⁰ it would lead to unnecessary repetition to enumerate them here. We shall confine ourselves, therefore, to a description of the respiratory tract lesions, and these, for the sake of brevity, are discussed collectively.

Lungs. It may be stated that the lungs differed in no way from the lungs of other influenzal patients. The left lungs varied from 490 to 1040 grams in weight and the right lungs from 590 to 850 grams. The anterior edges of the lungs were in each case moderately inflated, but this was never more marked than in other patients which did not have subcutaneous emphysema. In no case were air bladders or pearl-like distended air vesicles seen, although this was not infrequently encountered in our other influenza autopsies. The surface of the lungs was carefully examined to note any point of possible rupture, but this could in no instance be demonstrated. The posterior parts of the lungs were more or less consolidated, the areas of bronchopneumonia tending to become confluent. The extent of pneumonic involvement was never more marked than in the average influenza pneumonitis. The pleuritic complications were of the type usually met with. In no instance were the lungs firmly adherent to the lateral chest wall.

The cut surface resembled that usually seen in influenza pneumonitis, that is, it was generally very bloody and very moist, with large, poorly circumscribed, consolidated areas, some of which were granular, others entirely smooth. The bronchial branches, in all but one instance, contained large quantities of thick, creamy pus. The bronchial mucosa was swollen and deeply hemorrhagic. Once the walls of several of the larger bronchial branches were definitely eroded and the lumen markedly dilated, forming acute ulcerative bronchiectases (Fig. 5). In another instance cylindrical dilatation of some of the bronchial branches was present.

The microscopic examination of the lung presented the usual hemorrhagic, fibrinocellular exudate of influenzal pneumonitis. In all but one instance there were areas of necrosis, usually surrounding a destroyed bronchiole, but occasionally seemingly independent

¹⁰ Lucke, Baldwin, Wright, Toynbee and Kime, Edwin: Pathological Anatomy and Bacteriology of Influenza, Arch. Int. Med., August 15, 1919.

of the bronchial tubes. Once marked thickening of the inter-pulmonary septa occurred. The bronchial branches in each instance presented here and there partial or complete erosion of their walls, masses of necrotic debris and fibrin occupying the site of the destroyed areas. Once the peribronchial tissue was found markedly distended, giving the appearance that air had escaped through the destroyed bronchial wall in the loose peribronchial tissue (Fig. 6). While ulcerative bronchitis was not uncommonly met with in about 200 cases of influenzal pneumonitis, which we have examined here postmortem, it appeared regularly in the four cases complicated with subcutaneous emphysema. Ulcerative bronchiectasis of the larger bronchial branches was uncommon in the epidemic here, occurring only twice outside of the case reported here.

Bacteriological cultures were made during life from the subcutaneous tissues at various parts of the body, and after death from the lungs, pleural exudate, subcutaneous tissues, heart's blood, spleen, brain, and other organs. As has been stated in the clinical part of this communication, all the antemortem cultures were negative; the postmortem cultures presented in each case hemolytic streptococci, pneumococci, and influenza bacilli, either alone or in combination.

DISCUSSION OF THE MODE OF ORIGIN OF SUBCUTANEOUS EMPHYSEMA. It may be well to briefly review the various theories which have been suggested as the cause of this unusual complication:

Bacterial activity may be at once dismissed, since no local inflammatory reactions point to this condition. Torrey and Grosh speak of a destructive softening of the lung parenchyma, due probably to alteration of the lung tissue by toxin or virus. Chemical changes in the blood, permitting escape of air into the tissues is a possibility. The delayed time of the coagulation of the blood, the frequency of nose-bleed, petechial hemorrhages throughout the body, allows one to entertain the thought that chemical blood changes may occur which prevent the blood from maintaining the normal balance of its gases. We have analyzed the air obtained by puncture of the distended scrotum of one of the patients examined and found it to resemble atmospheric air.

Most of the writers who have reported cases of subcutaneous emphysema complicating influenza maintain that this condition is purely mechanical in origin. Thus, Symmers says, "In two cases rupture of the distended air vesicles has taken place probably near the apex of the lung. In another rupture occurred in the left pleural cavity, with the production of pneumothorax. In none of these cases was it possible to demonstrate at necropsy the actual point of rupture." Berkley and Coffen report 11 cases, 2 of which were associated with spontaneous pneumothorax. They suggest that subcutaneous emphysema may occur through the intrapleural route, providing that adhesions exist between the two layers of

pleura at the point of rupture, or through the extrapleural route if the air dissects its way to the hilum of the lung. Clark and Synnott, in the report of 12 cases, conclude that the origin of the gas was from weakened alveoli of the lung under pressure.

We believe that subcutaneous emphysema chiefly arises by escape of air from ulcerated or eroded bronchi and its passage along peribronchial or perivascular channels into the mediastinum. The clue of our explanation, in at least 2 of the cases, was found in the occurrence of marked ulcerative bronchitis and subcutaneous emphysema, both located on the left side.

If we disregarded simple mechanical rupture of peripheral alveoli as a highly improbable factor in the production of subcutaneous emphysema, there remain, then, only three possible ways for pulmonary air to reach the subcutaneous tissues: (*a*) by necrotizing destruction of alveoli; (*b*) by ulcerative or erosive rupture of a bronchus; (*c*) by rupture of pulmonary tissue through adherent pleural surfaces. By necrotizing destruction, alveolar air could pass into the loose peribronchial or perivascular areolar tissue and thence into the mediastinum. By ulceration or erosion of a bronchus the air would likewise gain the mediastinum. In neither case would the air pass into the pleura, because this is a closed sac. The third way is through perforation of necrotic pulmonary and overlying pleural tissue into the pleural cavity, resulting in pneumothorax. Should the visceral and parietal layers of the pleura adhere to one another the air could penetrate both layers and dissect the areolar tissue between the parietal pleural and thoracic wall to the mediastinum. Such a case would necessitate, it seems, a considerable area of adhesion. Once the air has found a vent from the pulmonary tissues, expiratory force and elasticity of the chest wall would further drive it along the lines of least resistance, which is into the neck (the location in which the subcutaneous emphysema apparently always began). Thence, along fascial planes, the emphysema would become generalized.

Microscopic examination⁷ presented a distention of the peribronchial areolar tissue (Fig. 6), and this we consider a support of our second explanation of the escape of air from the lung.

The question would naturally arise, "Why should this condition be so uncommon when ulcerative bronchiectasis is not infrequently met with in various diseases, as, for instance, tuberculosis. But it must be pointed out that bronchiectasis rarely occurs acutely and that the reaction of the tissues surrounding the bronchi would probably form a wall impenetrable to the air. It may be assumed, then, that only in rapidly occurring bronchiectasis, without sufficient tissue reaction, is such a condition possible, and that they arise but rarely. It would seem, likewise, that a fair-sized bronchial branch is necessary to allow sufficient air to escape for the production of emphysema. This would appear to us more likely as the cause than

mechanical rupture of peripheral alveoli, for not only are hugely distended and sometimes ruptured alveoli frequently encountered in both acute and chronic pulmonary emphysema, but the rupture of a few air sacs would not likely lead to a widespread air infiltration. Further, rupture of peripheral alveoli could only produce emphysema, provided that firm adhesions were present between the pleural layers at the point of rupture. Pneumothorax would result otherwise and in none of the cases reported has this occurred frequently. In the one instance where pneumothorax was present in our series, it was not at all marked, since only a few small air bubbles escaped upon puncturing chest wall through a pocket filled with water.

It is not at all unlikely that erosion or rupture in a bronchial tube might be overlooked, and this, we feel, rather strengthens than weakens our argument. The absence of mediastinal emphysema in two of our cases may be readily explained by the gradual absorption of air which occurred in every one of these cases, for, as has been stated, a marked reduction in the extent of the subcutaneous emphysema took place in every instance. This probably is due to the gradual closing up of the point of eruption because of cellular reaction.

CONCLUSIONS. 1. Subcutaneous emphysema is an exceedingly rare complication of influenza.

2. Previous explanations of the condition seem inadequate and unsatisfactory.

In two of our postmortem cases we encountered a combination of more pronounced left-sided subcutaneous emphysema with left-sided ulcerative bronchitis, and on microscopic examination the peribronchial tissue was found greatly distended. We believe the bronchial air to have escaped into the loose peribronchial tissues, and by dissecting along lines of least resistance to have gained entrance to the mediastinum and thence, along fascial planes, to the subcutaneous tissues. In this way the closed pleural sacs are not involved, and this accounts for the infrequency of pneumothorax in this condition.

ACKNOWLEDGMENT. We desire to thank Major W. W. Hamburger and Major Fox, respectively chiefs of the medical and laboratory services, for kind suggestions, and Captain Harris and Lieutenant Pedan for the roentgen plates.

GROSS PATHOLOGY OF INFLUENZAL PNEUMONIA IN FRANCE.

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THE material for this paper was collected from 106 autopsies on cases of pneumonia dying at a base hospital in France (Commercy,

Meuse). A few deaths occurred in December, 1918, the number increasing in January, reaching its highest point during the first two weeks in February and then gradually subsiding with scattered cases during March and April.

Only primary pneumonias have been included in this series and not pneumonias complicating typhoid fever, meningitis, traumata, etc.

PATHOLOGY. General. Of the skin manifestations, jaundice was the most common, occurring in 40 cases. Usually slight and only sufficient to stain the sclera, the skin of the face and perhaps the aorta, it was not infrequently deep enough to stain the subcutaneous and mediastinal tissues and the kidneys. Herpes of the lips appeared 8 times, 3 times with lobar pneumonia, 5 times with lobular pneumonia. Skin or conjunctival petechiæ were never seen. A well-demarcated erythema of the tip of the nose, without swelling or edema occurred once. It was first noted one day before death.

Emphysema of the subcutaneous tissues of the neck, chest and shoulders occurred four times. The gas that rushed forth on opening into such an emphysematous area was odorless and non-inflammable. This condition was usually associated with emphysema of the soft areolar tissues of the anterior mediastinum. Occasionally blebs were observed between the deeper layers of fascia covering the chest wall and beneath the pleura. None of these cases, however, was associated with hemolytic staining.

Palpable enlargement of the axillary lymph nodes, especially on the right side, occurred 12 times. The nodes were removed and examined in 2 cases but aside from enlargement showed no gross changes.

Changes in the recti muscles occurred in 35 cases. At times merely an unusual pallor, dryness and opacity were present. Such muscles seemed to have lost their elasticity, were brittle and very easily fragmented and torn. Though this condition was usually diffuse, uniformly involving a considerable portion of the muscle, at times small islands of diseased muscle, rather sharply demarcated from the surrounding normal tissue, were seen. Usually, hemorrhage into the muscle, with rupture of the fibers and hemorrhage between the muscle and its anterior and posterior sheaths, were also present. The hemorrhage frequently dissected down into the space in front of the bladder and could often be seen through the peritoneum as a blue mass bulging into the peritoneal cavity. In one case complete rupture of both recti was found. The torn ends of the muscles were separated a full finger's breadth. This peculiar degeneration of the recti usually involves the lower fourth of the muscle, although similar changes are often seen, either alone or together with change below, in the recti at their attachments to the ribs. Abscess never occurred.

An edema of the right arm, with slight reddening of the posterior surface of the forearm, occurred once. The arm veins were dissected but no thrombi found. In this case the axillary and cervical lymph nodes on the right side were considerably enlarged.

Purulent inflammation of the right sternoclavicular articulation and of one of the lower cervical intervertebral articulations was found once, complicating a case of lobular pneumonia, with multiple lung abscesses. Splenic culture was sterile, cultures of both lungs showed *Bacillus influenzae*, culture of the sphenoid and a pneumococcus.

Respiratory System. By far the most usual lesion encountered in the lungs was acute lobular pneumonia. The lungs were large, heavy and moist. On section one found, scattered throughout all the lobes usually, raised, granular, firm, grayish or red areas, about 5 to 10 mm. in diameter. The intervening lung tissue was red, moist and emphysematous. Occasionally dark red hemorrhagic areas, without consolidation, were seen. In one case intense congestion and edema of both lungs (from which the *Streptococcus hemolyticus* was grown in pure culture) was the only pulmonary lesion. The raised, granular areas were frequently confluent, especially in the lower lobes.

The next most frequent lesion met with in the lungs was lobar pneumonia. This differed from the lobar pneumonia met with in civil life in its bacteriology, streptococci being found in the lungs nearly as frequently as pneumococci, and in its not infrequent combination with lobular pneumonia.

Another type of pneumonia encountered occasionally (7 cases) was interstitial bronchopneumonia. These cases differed from those described by MacCallum in their bacteriology. One of the cases showed Gram-negative cocci in pure culture from both lungs and another showed staphylococci.

Empyema, as the predominating lesion, was found twice, serofibrinous pleurisy as the predominating lesion once, acute congestion of the lungs once and multiple abscesses once. Empyema, or purulent pleurisy, occurred but 4 times in the entire series. It was twice associated with multiple lung abscesses. Multiple lung abscesses were found 3 times.

The pleural cavities usually contained a few cubic centimeters of fluid. Hemorrhages into the pleuræ, both large and small, were very frequent. Fibrinous pleurisy occurred 28 times, serofibrinous pleurisy 12 times and empyema 4 times. The pleural fluid was frequently blood-tinged. The fibrinous exudate was usually small in amount, often merely an opacity on the surface of the lung. It was usually seen where the diseased lung tissue reached surface.

Bronchiectasis occurred three times, twice in the right upper lobe, once in the left lower lobe. Acute bronchitis was a very frequent accompaniment of the disease. It usually extended up

into the trachea, involving its lower half and fading out in its upper half. Purulent bronchitis was seen 5 times. Enlarged, soft, moist, reddish bronchial lymph nodes were found in 59 cases.

The larynx was examined in 38 cases. Congestion of the vocal cords (acute laryngitis) was found 6 times and edema of the epiglottis and arytenoepiglottidean folds twice. Occasionally hemorrhages into the mucosa covering the posterior surface of the epiglottis or thyroid cartilage were seen. Pharyngeal congestion was seen in a few cases. It was associated with a reddening of the base of the tongue and was sharply limited below at the commencement of the esophagus.

Circulatory System. Serofibrinous pericarditis occurred 6 times, purulent pericarditis once. Generally neither the quantity of fibrin nor fluid was abundant. It was always accompanied by acute pleurisy. The pericardium showed petechial hemorrhages in 49 cases.

Dilation of the heart was found in 43 cases, 31 times on the right side, 12 times on the left. The cardiac dilation was usually slight, the right ventricle perhaps occupying one-half the posterior surface of the heart instead of one-third, as it normally does. But occasionally it was marked and was twice associated with sudden death.

Cloudy swelling of the myocardium was found in 51 cases. The heart muscle was pale, soft and opaque. Occasionally a real flabby, thinned-out heart wall was seen, but this was rare. Acute vegetative endocarditis was found 4 times. The vegetations were small, always on the mitral valve, twice on chronically diseased valves, twice on otherwise normal valves. Hemorrhages into the cusps occurred in 7 cases, usually into the mitral valve, occasionally into the tricuspid and aortic valves.

In 3 cases the intima of the aorta was swollen, sticky and easily detachable (acute aortitis). Atheroma of the aorta and coronaries was noted in almost every case. It was, however, found with equal frequency in patients dying from other acute infections and from traumata.

Hemolytic staining of the endocardium or pericardium or both was observed 5 times. Most of these cases were autopsied twenty-four hours or more after death, although in one case autopsy nine hours after death revealed slight hemolytic staining of the endocardium.

Liver. Cloudy swelling of the liver was found in 85 cases, congestion 9 times. The cloudy swelling was usually very marked.

Spleen. Large, soft spleen was observed in 65 cases. The enlargement, as a rule, was not marked; the spleen was usually reddish and the Malpighian bodies were usually indistinct.

Genito-urinary System. Cloudy swelling of the kidneys was found in almost every case. It was usually well-marked. Renal congestion was also frequent, occurring in 37 cases. Acute nephritis

occurred 4 times, miliary abscesses of the kidneys once. Bile-staining of the kidneys in cases of deep jaundice was frequent. Microscopic sections of the kidneys in 3 cases, chosen at random from those showing cloudy swelling grossly, showed necrosis and desquamation of the tubular cells (convoluted tubules mainly), duplication of the tubular epithelium with hemorrhage into the tubular lumen, apparently a true acute tubular nephritis. The glomeruli, aside from congestion, were normal.

Hemorrhages into the renal pelvis occurred in nearly 50 per cent. of the autopsies (52 cases). The hemorrhages were usually small, but occasionally they were quite large, especially in the calices beneath the tips of the pyramids. The hemorrhages extended for a short distance into the ureter, but were never seen below the upper fourth. Hemorrhages into the bladder wall were noted 6 times.

Occasionally, on opening a testis, bloody fluid was seen. The prostate showed no changes.

Adrenals. Cloudy swelling of the adrenal cortex was seen in 23 cases. Congestion of the medullary substance was frequent. Hemorrhage into the medulla occurred 3 times. It was bilateral once, unilateral twice.

Thyroid. The thyroid was examined in 38 cases. Cloudy swelling was found 12 times.

Gastro-intestinal Tract. The gastro-intestinal tract showed few changes. Acute fibrinous peritonitis was found once. In this case the peritoneum covering the lower ileum was reddened, hemorrhagic and covered by a fibrinous exudate. The solitary lymph follicles and Peyer's patches were raised and reddened. Bloody intestinal contents were found once. Prominence of Peyer's patches and solitary lymph follicles, especially the latter, with or without reddening, were frequently noted in cases in which no other evidence of status lymphaticus was found. Acute appendicitis occurred once.

The cranial contents were examined in 26 cases. Meningitis was never seen. Cases of meningococcic meningitis, complicated by pneumonia, have not been included in this series. One case of pneumococcus Type I meningitis came to autopsy. The lungs showed an early lobular pneumonia of the left lobe. Aside from a very delicate tegmen tympani on the right side the search for an explanation of the infection was negative. The middle ears and sinuses were clear and the blood culture at autopsy sterile.

The brain often showed flattening of the convolutions and narrowing of the ventricles.

The sphenoid sinus was opened 22 times. Purulent fluid was found 18 times, serous fluid twice and in 2 cases no change was observed. Purulent frontal sinusitis and purulent otitis media were seen frequently, but no note of the number of examinations was made.

RESULT OF POSTMORTEM CULTURES.

Predominating organisms.	Number of cases.	Percentage of cases.
<i>Streptococcus hemolyticus</i>	18	32.0
Pneumococcus:		
Type I	3	5.2
Type II	2	3.5
Type III	1	1.7
Type IV	4	7.0
Not typed	6	10.5
	16	28.0
<i>Staphylococcus</i>	9	15.5
Non-hemolytic streptococcus	5	9.0
<i>Bacillus influenzae</i>	5	8.5
Gram-negative cocci	4	7.0
Total	57	100.0

BACTERIOLOGICAL NOTE. Thirty-five cultures were made from the circulating blood taken from the arm vein in the usual way. Of these 3 showed the pneumococcus Type I, 2 the pneumococcus Type IV, 2 pneumococci type undetermined and 1 the meningococcus. In 2 cases of lobar pneumonia, in which pneumococci were isolated from the blood during life, postmortem cultures from the lungs yielded the *Streptococcus hemolyticus*. It is probable that in these 2 cases at least the *Streptococcus hemolyticus* was a secondary invader.

The results of the postmortem cultures are shown in the accompanying chart. The Gram-negative cocci, which were found alone and frequently together with other organisms, resembled meningococci both morphologically and culturally, but they failed to agglutinate with polyvalent automeningococcus serum. Cultures from the sphenoid sinus gave very satisfactory results, the organism found there generally corresponding to the organism found in the lungs or blood.¹

I wish to express my thanks to Dr. J. J. O'Leary, Detroit, who did a considerable part of the postmortem bacteriology.

SUMMARY. 1. During January and February, 1919, an epidemic of severe lobular pneumonia occurred about the region of Commercy, France, accompanied by jaundice, cloudy swelling of the parenchymatous organs and heart muscle and hemorrhages into the pericardium, renal pelvis and other viscera.

2. Changes in the rectus muscle were observed in 33 per cent. of the cases.

¹ The case in which the positive meningococcus blood culture was obtained, was clinically lobular pneumonia. There were no signs of meningitis and a lumbar puncture did not seem advisable. The patient recovered. The organism was grown in plain infusion broth to which the blood had been added after five days' incubation. The organism was typical morphologically and culturally and was agglutinated by polyvalent antimeningococcus serum, dilution 1 to 200 and failed to agglutinate in normal sera. It was not typed.

GROSS PATHOLOGICAL FINDINGS.

	Number of cases.	Percentage of incidence.
Number of autopsies	106	
Jaundice	40	30.0
Herpes	8	7.5
Subcutaneous emphysema	4	3.7
Degeneration of recti	35	33.0
Edema of arm	1	0.9
Purulent arthritis	1	0.9
Enlargement of axillary lymph nodes	12	11.3
Respiratory system:		
Lobular pneumonia	77	72.6
Lobar pneumonia	14	13.0
Interstitial pneumonia	6	5.6
Lobar and lobular pneumonia	5	4.7
Interstitial and lobular pneumonia	1	0.9
Multiple lung abscesses	3	2.8
Fibrinous pleurisy	28	26.2
Serofibrinous pleurisy	12	11.3
Empyema	4	3.7
Bronchiectases	3	2.8
Acute bronchitis	82	77.0
Purulent bronchitis	5	4.7
Large, soft bronchial lymph nodes	59	55.0
Number of larynges examined	38	
Acute laryngitis	6	15.7
Edema of glottis	2	5.2
Heart:		
Serofibrinous pericarditis	6	5.6
Purulent pericarditis	1	0.9
Petechial hemorrhages in pericardium	49	46.2
Cloudy swelling of heart muscle	51	48.0
Cardiac dilatation—right	31	29.0
Cardiac dilatation—left	12	11.3
Acute endocarditis	4	3.7
Hemorrhage into cusps	7	6.6
Hemolytic staining of endocardium	5	4.7
Acute aortitis	3	2.8
Liver:		
Cloudy swelling	85	80.0
Congestion	9	8.4
Large, soft spleen	65	61.0
Kidneys:		
Cloudy swelling	93	87.0
Congestion	37	34.8
Acute nephritis	4	3.7
Miliary abscesses	1	0.9
Hemorrhages into renal pelvis	52	49.0
Hemorrhages into bladder wall	6	5.6
Adrenal:		
Cloudy swelling	23	21.6
Hemorrhage	3	2.8
Thyroid:		
Number of times examined	38	
Cloudy swelling	12	31.5
Gastro-intestinal tract:		
Fibrinous peritonitis	1	0.9
Sphenoid sinus:		
Number of cases examined	22	
Serous sinusitis	2	9.0
Purulent sinusitis	18	81.8

3. Empyema was rare, occurring in less than 4 per cent. of the cases.

4. Acute laryngitis was comparatively rare, occurring in but 6 out of 38 larynges examined (16 per cent.).

5. Sphenoid sinusitis was a very common complication and was found in 20 out of 22 cases examined (90 per cent.).

6. Seven out of 35 premortem blood cultures showed pneumococci. The rest were sterile with the exception of one, which showed a meningococcus.

7. The bacteria found in the organs at autopsy were varied, the *Streptococcus hemolyticus*, pneumococcus, staphylococcus, non-hemolytic streptococcus, *Bacillus influenzae* and Gram-negative cocci being found in the various cases in the order of frequently given above.

CHRONIC NON-TUBERCULOUS LUNG INFECTION.

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THE material for this paper consists of eight cases from a somewhat larger number seen during the past year in the medical clinic of the University Hospital of the State University of Iowa. Our object has been simply to review the literature and to emphasize some points in the diagnosis and treatment of this condition which so closely resembles tuberculosis and which is so frequently erroneously diagnosed as such. We do not claim any originality either in diagnosis or treatment, both of which have previously been fully described.

The recent influenza epidemic left in its wake countless cases of chronic cough, many of which are unquestionably due to tuberculosis, as is proved by the finding of acid-fast bacilli in the sputum. However, in many so diagnosed tubercle bacilli are not found and the subsequent course is unlike tuberculosis. Many of these cases are simple bronchitis, general or localized, or, to use the term recently suggested by Garvin, Lyall and Morita,¹ chronic non-tuberculous lung infection.

In 1902 and 1905 F. T. Lord² described a series of these cases under the title of chronic influenza. Since then similar cases have been reported by Riesman³ in 1913, Larabee⁴ in 1915 and more recently papers on the subject have appeared by Hammond and

¹ *Am. Rev. Tuberculosis*, 1917, i, 16.

² *Boston Med. and Surg. Jour.*, 1902, cxlvii, 662; *Boston Med. and Surg. Jour.*, 1905, clii, 537.

³ *AM. JOUR. MED. SC.*, 1913, cxlvi, 313.

⁴ *Boston Med. and Surg. Jour.*, 1915, clxxii, 257.

Wollman,⁵ Garvin, Lyall and Morita and J. A. Miller.⁶ The disease has been variously called "a lobular form of bronchopneumonia of long duration," "localized bronchitis," and "subacute and chronic non-tuberculous lung infection."

ETIOLOGY. *Age.* The onset may occur at any age, but seems to occur somewhat more frequently in children. G. F. Still,⁷ who has described this disease in children, says it is most frequent before the age of five, due not only to the frequency of measles and whooping-cough, which diseases it often follows, but because of a special predisposition of the bronchi of children to infection. In children there is a relatively large amount of loose connective tissue in the walls of the bronchi and alveoli, which is easily infected and permits chronic dilatation of the bloodvessels to occur with relative ease. The frequency of mouth-breathing and chronic nasal disease in children also undoubtedly increases their liability to bronchial disease. Of our 8 cases, 3 began before the age of six, 2 at thirteen and 3 at twenty. Miller's cases ranged from seven to sixty years. The majority of Riesman's cases were between ten and twenty.

Sex. The disease is more common in females. In Miller's series there were 14 females to 8 males. In Riesman's series girls predominated. Our cases were divided equally between the two sexes.

Previous Infection. The syndrome usually follows acute diseases, which affect particularly the upper respiratory tract, such as measles, whooping-cough and influenza, though in some cases it comes on insidiously.

Season. Both the onset and the exacerbations occur more frequently during the colder months, October to April, due probably to the crowding of people together in poorly ventilated and often dusty or smoky rooms and the increased tendency for respiratory disease to pass from person to person under such circumstances.

Nasal Disease. Adenoids and nasal deformities which cause mouth-breathing are important etiological factors. Chronic sinusitis is probably present to a greater or less extent in all the cases. Three of our cases had definite severe sinus diseases and in all the lung exacerbations were invariably accompanied by coryza.

Family. Miller reports 2 cases from the same family in two instances. In each instance the same organism was isolated from the 2 cases, suggesting the possibility of contagion. Two of our cases came from the same home and *Staphylococcus albus* was isolated from the sputum of each of them. The same predisposing factor, as poor ventilation, with dust or smoke, may help in increasing the family incidence.

Deformed Chest. Still mentions the frequency with which localized bronchitis may occur in rachitic chests, due to the fact that

⁵ Tr. Nat. Assn. Study and Prev. Tuberculosis, 1916, p. 171.

⁶ AM. JOUR. MED. SC., 1917, cliv, 805.

⁷ Common Disorders and Diseases of Childhood, p. 353.

portions of the lung cannot properly expand and easily become chronically infected. None of the cases here reported had any deformity of the chest whatever, but we have seen some cases in which the deformity seemed to be of etiological significance.

Bacteriology. Bacillus influenzae is the most frequent predominating organism in the sputum and was found in 36 per cent. of Lord's cases, but any of the common invaders of the respiratory tract may be found. In our 8 cases Bacillus influenzae was found to predominate in only one instance, while the Streptococcus pyogenes was predominant in 3 and Staphylococcus albus in 4. In one of the streptococcus cases a similar organism was isolated from pus found in the antrum of Highmore. Miller's cases showed Bacillus influenzae in 7, pneumococcus, type IV, in 10, and Streptococcus viridans in 4.

Out of 66 cases Lord found Bacillus influenzae in 44, pneumococcus in 8, Micrococcus catarrhalis in 5, Bacillus mucosus capsulatus and pseudopneumococcus in 3 each. A different organism is sometimes found to predominate at a later time, as was the case in one of our patients who had Bacillus influenzae at first; but two weeks later Staphylococcus albus was found to be the predominating organism. Lord found such a change to occur in some of his cases.

Pathology. Since this is a relatively benign process there has been very little opportunity to make postmortem examinations. None of our cases came to autopsy. Hammond and Wollman had an autopsy on one case and found "localized bronchitis and infiltration of the bronchial wall and foci of bronchopneumonia about the smaller bronchi." Lord examined, postmortem, a typical case of forty-four years' duration and found slight general bronchiectasis, with many small areas of interstitial pneumonia. It therefore seems probable that, as Miller has stated, the pathology "may consist of a localized bronchitis, with a lobular distribution, which may clear up or persist in a subacute form, offering a site predisposed to exacerbations and increased tendency to fibrosis." That the late changes are bronchiectasis and areas of interstitial pneumonia is shown by Lord's case. The tendency in some of the cases for the cough to become paroxysmal, with considerable amounts of sputum, shows there must be some dilatation of the smaller bronchi fairly early in the course of the disease. The roentgenograms often show some fibrous thickening, which occasionally pulls the heart slightly to the affected side.

SYMPTOMS AND COURSE. Chronic cough, usually most marked in the mornings, and expectoration of variable amounts of mucopurulent sputum are the outstanding features in practically all the cases. The general health is relatively little affected, but many of the cases complain of slight loss of appetite, slight loss of weight and lack of endurance. Four of our cases complained of these, but the other four claimed they were in perfect health except

for cough and expectoration. One of our cases had several frank hemorrhages, two of which consisted of as much as a pint of bright red blood. Many cases with hemoptysis have been reported in the literature. Moderate fever, night-sweats, pain in the chest, in short, any of the symptoms of tuberculosis may be present. Riesman has pointed out that subacute and chronic lung infections may be the cause of obscure long-continued fever, as some of these cases complain of no symptom referable to the chest, and it is only by making routine chest examinations and finding the typical signs that the nature of the process is suspected.

The course of the disease is marked by extreme chronicity, with a tendency to frequent exacerbations. The latter are usually accompanied by coryza, fever, increased cough and tightness in the chest, frequently pain in the affected side, and occasionally, as in one of Miller's cases, slight effusion. Some of the cases go on to complete recovery in from two to six months, but when the condition has become well established the patients go on from year to year with nothing but temporary abatements, and eventually the general health becomes more or less impaired. The prognosis is best in children.

PHYSICAL SIGNS. The site of the lesion in our 8 cases was the left lobe in 5, the right lower lobe in 1 and both lower lobes in 2. In 7 of Lord's chronic cases the right lower was affected in 2, the left lower in 1 and one or both apices in 3. Garvin, Lyall and Morita state that in 90 per cent. of the cases the lesion is in the lower half of the lungs. Inspection reveals nothing abnormal, or, at most, only slight lagging of the affected side. The typical signs are subcrepitant rales, especially after cough, in one of the lower lobes. These may be brought out by placing the patient in the inverted position, as has been emphasized by Garvin, Lyall and Morita. Over the affected area the percussion note is often somewhat impaired and the breath sounds somewhat harsh. Physical signs are frequently insignificant and occasionally entirely absent.

Three of our patients were rather pale, emaciated and "sick" looking, but all the rest were well nourished and of good color. Two had considerable incurvature of the finger nails. All had slight leukocytosis (11,000 to 12,400 per c.mm.) and three had slight anemia.

All of our cases raised mucopurulent sputum varying in amount from $\frac{1}{2}$ dram to 1 ounce daily. Two cases were not expectorating anything when admitted, but upon being placed in the inverted posture for fifteen minutes, three times a day, both began bringing up small amounts of mucopurulent sputum. The sputum in most of our cases contained the green nummular masses so often seen in influenza. Tubercle bacilli were never found in any of the sputa after repeated examinations both with and without antiformin.

The von Pirquet test was negative in the four children. Two of

the adult cases gave no general or focal reaction to the subcutaneous test. The latter test was not tried on the other two adult cases.

DIAGNOSIS. That the diagnosis is frequently missed is shown by the fact that one-half of our cases were previously diagnosed tuberculosis. Cases with chronic cough, which is not paroxysmal; purulent sputum persistently negative for acid-fast bacilli; insignificant roentgen-ray findings, with rales located in the lower half of the chest (in the absence of a heart lesion); and the general health only slightly impaired are undoubtedly cases of chronic non-tuberculous lung infection.

When the lesion is located at one or both apices the diagnosis is more difficult and tuberculosis cannot always be positively excluded even after prolonged observation. Against the latter, however, is the fact that the disease has no tendency to spread to other parts of the lung and the sputum never contains tubercle bacilli. The absence of acid-fast bacilli from purulent sputum, after careful and persistent search, can be said, for all practical purposes, to rule out tuberculosis. The general robustness of the patients in spite of the extreme chronicity of the disease and the frequent exacerbations, the negative roentgen-ray finding and negative tuberculin test are sufficient evidence to exclude tuberculosis.

In our 4 cases which were previously diagnosed tuberculosis the signs were entirely confined to the lower half of the lungs. Basal lesions in tuberculosis are rare and are always toxic. The good, general health of these patients, in relation to their rather extensive physical signs of lung involvement, made us doubt the diagnosis at once.

Subacute cases, with moderate daily rise of temperature, may at first resemble typhoid fever; but the slight leukocytosis, negative Widal and blood culture, together with the finding of the characteristic lung signs, should suggest the correct diagnosis.

Bronchiectasis can usually be excluded by the fact that the sputum is brought up in smaller amounts and not in the paroxysmal manner so characteristic of that disease. However, as mentioned before, sooner or later some of the cases probably develop slight bronchiectasis.

Sometimes the disease may be recognized at its very beginning by careful examination before discharge of all cases of influenza, acute bronchitis, measles, etc. Recently one of our patients with acute bronchitis, who had never been troubled with cough before, was about to be discharged after being free from temperature and symptoms for several days. On routine examination of the chest the left lower lobe was found to be filled with crackling rales, and the percussion note was somewhat impaired over this area.

During the six weeks since he has been reporting regularly to the out-patient clinic, and, in spite of treatment, the signs still persist, and he has now considerable cough and expectoration.

TREATMENT. As Garvin, Lyall and Morita have pointed out the essential treatment is posture. The constant hacking which these patients carry on never entirely frees the smaller bronchi from secretion and alleviates the desire to cough for only a brief period of time. Drainage can be accomplished by having the patient hang over the end of the bed or kneel on a chair, with his hands on the floor. Placing the patient in the Trendelenburg or reverse Trendelenburg position on an operating or treatment table is more comfortable for the patient, and in some cases produces better drainage. The posture should vary somewhat, depending upon which part of the lung is to be drained. It may be necessary to try several different positions before the one which accomplishes adequate drainage is determined. The experience of the patient is often valuable in making this determination. The treatments should be of sufficient length and frequency to keep the affected area fairly free from secretion. Fifteen minutes, three or four times a day, are usually necessary at first. All of our cases have received distinct benefit from this form of treatment. Patients who have been coughing more or less all day long, and even having their sleep disturbed by paroxysms of coughing, soon cough only at the time of inversion. The amount of sputum gradually becomes less and the general health rapidly improves. There may be a slight febrile reaction after the initial drainage, but after that the toxic symptoms rapidly disappear entirely. Two of our cases who were raising no sputum began to expectorate from 1 to 4 c.c. daily after postural treatment was started, thus giving us an opportunity to examine the sputum in addition to putting an end to their cough and afternoon fever. During or immediately after inversion the rales can be much more easily heard, and, in fact, may be heard only at this time.

It may be necessary to continue this inversion over long periods, a year or more, but patients soon become accustomed to it, and the benefit is so obvious that they are usually enthusiastic and can readily be persuaded to carry it on in their homes. Our patients also received inhalations of compound tincture of benzoin following the inversions. In view of the fact that the affected part of the lung may be held down by adhesions, pulmonary gymnastics in the form of blowing-bottles should benefit some of the cases. This has been tried, with considerable success, in this hospital in the department of pediatrics, where a number of these cases have occurred. In all the cases the nasal sinuses should be carefully examined and any existing disease eradicated as far as possible.

Since the exacerbations occur in the colder months it may be advisable to recommend a warm climate for the chronic cases that are refractory to treatment. Exacerbations should be avoided by living an out-of-door life and avoiding exposure to people suffering from acute colds. Irritants to the bronchial mucosa, such as tobacco smoke and dust, should also be avoided.

We used an autogenous vaccine in 2 cases, but noticed no more improvement than in similar cases which were receiving only postural treatment.

I beg to acknowledge my appreciation to Professor C. P. Howard for giving me the opportunity to study and report these cases.

CASE REPORTS.

E. S., No. 6275. White boy, aged fourteen years, entered May 19, complaining of cough and expectoration dating from measles at five. He was well nourished and there were subcrepitant rales in both lower backs as high as the angles of the scapulæ. The sputum was negative for tubercle bacilli and the cultures showed a marked predominance of the *Streptococcus pyogenes*. Afternoon temperature, 99.6° F.; leukocytes, 11,000; Wassermann, von Pirquet and roentgenograms negative; chronic empyema of antrum of Highmore. Antrum was drained and reverse Trendelenburg posture for fifteen minutes, three times a day, were given. Discharged June 20, free from cough, expectoration and temperature.

O. M., No. 6337. Male, aged twenty-two years, entered June 4, with headache, cough and temperature of 102.8°, which began the day before. Past pulmonary history negative. Lungs negative. Temperature became normal on the sixth day but continued to raise large amounts of green nummular sputum, slightly streaked with blood. At this time the left lower lobe was found to be filled with subcrepitant rales. Six weeks later, when seen in the outpatient clinic, the signs were unchanged and the sputum contained a pure culture of *Bacillus influenzae*. He is now rapidly improving on postural treatment.

E. C., No. 6274. White male, aged nineteen years, entered May 19, complaining of constant cough and expectoration dating to whooping-cough, two years ago. During the last four months he had lost ten pounds and felt weak and tired. He was pale and emaciated. The lung signs were sharply localized to the right lower lobe, where the percussion note was impaired and many subcrepitant rales were heard. The sputum showed *Streptococcus pyogenes* and no tubercle bacilli. Afternoon temperature, 99.2° F.; leukocytes, 11,000; von Pirquet and roentgen rays negative. Carried out postural treatment at home. Two months later cough and expectoration had ceased and general health was much improved.

A. De S., No. 6114. White male, aged twenty-six years, entered April 3, 1919. Had constant cough, with frequent exacerbations and variable amounts of thick, yellow sputum as long as he could remember. Color and nutrition were normal and both lower lobes filled with rales. He was raising about one ounce of sputum daily, which contained a predominance of *Staphylococcus albus*. Afternoon temperature, 99.2° F., Wassermann, von Pirquet and roent-

genograms were negative. Chronic pansinusitis. Drainage of the sinuses and postural treatment for one month resulted in marked improvement in the cough and reduction of the daily amount of sputum to $\frac{1}{2}$ c.c.

E. B., No. 5810. White girl, aged fifteen years, entered January 10, 1919. Had been coughing since measles at six. Expecto-rated one dram to an ounce of sputum daily. Color and nutrition normal. Both lower lobes were filled with rales brought out by coughing. Afternoon temperature, 99.6°; leukocytes, 12,200; red cells, 3,910,000; hemoglobin, 75 per cent. Sputum was green nummular type and cultures showed *Staphylococcus albus*. Wassermann and von Pirquet negative. Roentgen rays showed considerable fine radiating thickenings at the bases. Sinuses negative. After two months of postural treatment the anemia had disappeared and she had gained six and three-quarter pounds. Cough, sputum and lung signs had disappeared.

L. C., No. 4816. White female, aged fourteen years, entered June 16, 1918. Had a chronic cough since whooping-cough in July, 1917, which had become much worse since she had measles in May, 1918, since when she has expectorated about one ounce of sputum daily, perspired profusely at night and lost weight and strength. She was very pale and emaciated and there was slight clubbing of the fingers. There was impaired percussion note and numerous moist rales over the left lower lobe. The sputum contained *Streptococcus pyogenes*. Roentgen rays, von Pirquet and Wassermann negative. Afternoon temperature, 99.2°; leukocytes, 11,000. Was discharged July 25, 1918, free from cough and expectoration. She had gained six pounds; color and temperature were normal.

L. E., No. 6299. White female, aged twenty-seven years, entered May 24, 1919. Had a severe cold eight years ago, during which she had several hemoptyses, two of which were as much as a pint. Has had constant cough since. Sputum is often blood-streaked. She looked healthy and the only signs found were impaired percussion note and moist rales over the left lower lobe. She was not expectorating when admitted, but after postural treatment was begun she raised one dram daily of green nummular sputum which contained *Staphylococcus albus*, and the cough ceased except at time of inversion. Subcutaneous tuberculin test and roentgenograms were negative.

E. D., No. 6374. White boy, aged thirteen years, entered June 16, 1919. Had whooping-cough at nine and has since had cough and expectoration, with frequent exacerbations. He was pale and emaciated and running an afternoon temperature of 99.8° The lower left lobe was filled with rales. Leukocytes, 12,000. Von Pirquet and roentgen rays negative. Sputum contained *Staphylococcus albus* in almost pure culture. Temperature and weight became normal and cough and expectoration much improved after two weeks.

**A PSYCHOLOGICAL THEORY OF THE CAUSE OF EPILEPSY,
WITH SPECIAL REFERENCE TO AN ABNORMAL
MUSCULAR EXPRESSION OF A STRONG
EMOTIONAL DRIVE.**

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EPILEPSY, though it has existed and has been studied as long as we have written history, is so complex in its phenomena that it has baffled the medical profession in establishing its etiology. It is now broadly defined as a chronic progressive disorder characterized by recurrent abrupt attacks of loss or impairment of consciousness with or without convulsions and accompanied oftentimes by a physical and by a mental deterioration. Recent medical investigation, since there is no definite pathology known common in every such case, has been an attempt to study the disease process chiefly from the viewpoint of a mental disorder.

In every individual case of epilepsy we find certain peculiar but definite mental characteristics which are common to all so afflicted. The mind of the epileptic is filled with thoughts and feelings of an unpleasant nature, so that he is seldom if ever happy. He is constantly wanting something that he cannot get. In his efforts to gain the thing desired, he possesses a strong determination that is characteristic only of his type of mentality. Although physically and mentally he is entirely incapable of attaining the things he desires, he possesses an unreasonable confidence in his own ability to overcome any obstacle. Failing to do so, he becomes temperamentally a misfit wherever found. He is sensitive about his incapability, which he will not recognize, is apt to be irritable when approached and becomes a patient subject to tantrums and even acts of violence when not managed with the greatest degree of caution and understanding. Wrapped up in his likes and dislikes of the unobtainable, he can usually be expected to miss the pleasure that he might find in performing tasks within the scope of his capabilities. This mental make-up, characterized by supersensitiveness, egocentricity and emotional poverty, does not help the epileptic to make proper adaptations in life.

We might conclude that given an individual with such an emotional constitution plus a particular type of stress we should get a particular epileptic reaction. Such a generalization, while it may be true, leads us into conditions difficult to explain. Every person, to a greater or lesser degree, manifests these same mental peculiarities and also is subjected to most every form of stress, so we shall have, then, to consider everyone, both young and old, as potential epileptics. The surgeon may, though he probably looks

forward with hopes to the time when he will not be asked to operate to relieve epilepsy upon clinical advice of such a doubtful nature as is given today, want more definite proof that the phenomenon is purely an abnormal mental reaction. Perhaps also we should consider that the many theories advanced by the internist, based on subjects as yet not well understood, such as endocrinic disturbances, intestinal intoxication, acidosis and increased intracranial pressure, may have an element of importance, since they probably deal with a resultant abnormal physiological process. These are steps made in the right direction and, like institutions, they are neither made nor destroyed in a day but must stand until supplanted by something better. Therefore, we must have here more than a generalization. We must, by a proper analysis, show the particular factors in a mental process that produces an epileptic reaction and show how it may be avoided.

A proper analysis of a mental, diseased state presupposes a working knowledge of normal mental activity. This is just as true as it is in the field of pathology, where we must first know normal tissue before we study the abnormal. Likewise, we study the physiology of the normal body before we investigate abnormal physiological processes. So any study of this subject, if it be of import, must show how the mental life of the epileptic differs from the mental life of a normal individual and consequently brings about his destruction.

Mental life is primarily teleological. Our inner faculties, that is, our instinct and ways of thinking, feeling or desiring, come to us when things interest or excite us, and they act as the motive power, which, when directed in natural channels, serve to secure our common welfare and safety. These feelings may, however, when improperly directed, find expression in an abnormal manner, and if habitually exercised in this way, may lead to the possessor's destruction.

Every mental state of this kind has a muscular expression. We recognize them in the voluntary and involuntary muscular reactions. We have, as an example of the latter, inconspicuous changes in breathing, in circulation, in general muscular tension and visceral changes, brought on by various emotional states. A definite feeling of this kind, which drives both voluntary and involuntary muscles to action, is hunger. We get hungry, go about getting something to eat and then find pleasure in eating as our hunger is satisfied. So these feelings, whether we are conscious of them or not, produce muscular activity which is brought about to meet some particular adaptation essential to the body's welfare.

Feelings which stir up voluntary muscular reactions are apt to be more keenly felt. Danger, for example, fills us with fear and the natural expression of this emotion is to exert our muscles in such a manner that we shall escape it. Flight is quite often the usual action

taken. If by running away we escape the danger, we experience a sense of pleasure in our success. While running, though, should we feel a doubt of our success in escaping the pursuing danger, our experience is very unpleasant, and the greater our doubt the greater is our fear, so we are able to run all the faster.

Another mental state which exemplifies a muscular expression of the voluntary type is seen in the reaction that follows anger. The natural expression of this emotion is to overcome the thing which causes the anger. Perhaps it means a fight. It is an interesting observation that, in a large, open field a man cannot fight as hard as he can when he is cornered. In the open he has plenty of room to maneuver, with the possibility of turning in flight if the battle grows too strong. Cornered, he has less space for maneuver, with no chance of escape except by overcoming his adversary. In this case the emotional feeling which gives him motive power for his efforts is not weakened by conflicting thoughts, but is made stronger by the increase of impending danger.

We cannot consider here all of our thoughts and feelings or whatever other names we may give our mental states, for they are infinite in number. We can, however, from our knowledge of them, draw this general conclusion: that they are, whether we are conscious of them or not, the motive power behind our efforts to do or to get things for ourselves or for those in whom we are interested. With such motive force calling for expression, five different ways are found as an outlet for these feelings. When we want to do or get something we may be:

1. Successful.
2. Unsuccessful—suicide.
3. Unsuccessful—cease trying.
4. Unsuccessful—insanity.
5. Unsuccessful—epilepsy.

Probably no life is so unpleasant as never to experience success in some degree. Nevertheless, to be successful in everything one attempts is doubtless a greater pleasure than anyone has ever experienced. So we mention the first manner in which feelings may find expression only as an ideal never reached.

The second also has little interest for us except that we must accept it as a frequent outcome to ill-success. Suicide is an abnormal manner of escape, but one that places the one who considers life not worth living, if he cannot do or get the particular thing of sole interest to him, soon beyond burden to others.

In the third we have to consider the action of the normal man who meets unsurmountable obstacles. Wanting to do or get something, he puts forth every reasonable effort. As he ponders and studies, perhaps worrying a little more than he should over his troubles, seeking some new way of approach that he may be successful, he soon feels the repulsiveness of greater effort in the face of the

futility of any attempt, so he ends the unpleasant experience by turning to other tasks which he can accomplish and thus finds pleasure in their success. The instances in which the normal man gives up when demands become too trying are as many and as varied as there are interests in life.

The fourth way of meeting a difficulty is a manifestation seen in insanity. In this condition, often complicating epilepsy, we do not find an individual who has formed the habit of avoiding the danger of too great mental stress as the normal man meets it. Instead, the unnatural habit is made of escaping an intolerable situation of unsurmountable circumstances through a mental state made more tolerable in a world of imagination, where hallucinations, illusions and delusions play a make-believe part.

The fifth and final way in which the motive power of emotional life finds expression, when the natural pleasurable channel of success is blocked, is through an epileptic reaction. Possessed with a mental make-up characterized by egocentricity and an emotional poverty for feelings not particularly concerned in his immediate desires, the epileptic, like the man cornered, has no possibility of escape except to accomplish what he desires or succumb in his efforts. He could avoid the latter outcome if he did not possess such an exaggerated notion of his own ability, and like the normal man could give up trying. But he labors on with every obstacle serving to aggravate his emotional drive to the point of an abnormal explosion.

Fatigue is a natural consequence of any mental activity, and it demands rest which we get normally when we sleep at night. If, however, the mental work is of the nature of violent strain, such as is experienced in extreme emotional effort, an abnormal degree of fatigue or exhaustion is had which calls for an immediate cessation of function until a period of rest intervenes. This is what happens in the phenomena of epilepsy when the patient falls unconscious. The higher brain centers which have to do with the directing and with the consciousness of efforts become exhausted from overwork when subjected to extreme nervous tension. This loss of consciousness is not deep enough to involve the motor centers, so the emotion goes on to an abnormal expression in muscular activity, unguided and uncoördinated, which we know as a convulsive seizure.

Two cases of this kind, which, from all the evidence gathered from the patients and their friends who knew them in the army, were the first attacks suffered of the kind, came to my notice while in France. The first was that of an excellent soldier of the infantry, an Armenian with our army, who had difficulties with the first sergeant of his company. The sergeant, of German parentage, possessed many racial characteristics. Although a fine specimen of physical manhood and an excellent American soldier, his very

appearance was odious to the Armenian, who had lost his wife and children in the massacres of his native land. Because of these differences, the Armenian was detailed to the officers' mess for duty, where he would be less apt to come in contact with the first sergeant. Some time later, however, their quarrel was renewed, when the first sergeant, in language which betrayed not a long separation from that of the Fatherland, proceeded to give the Armenian a lecture on proper respect to the first sergeant of the company. Angered to the breaking-point, the Armenian would have crushed him had he dared to violate the laws of military discipline; but inhibited, he faced his aggressor until in emotional exhaustion he fell unconscious, and the emotion went on to an abnormal expression in a typical grand mal attack.

The second case was that of a sturdy soldier at the port of embarkation for home. Burning up with the desire of getting home, an emotional state of feeling, known only to those who have experienced it, the soldier met difficulties because of a lesion of a suspicious venereal nature. Having passed daily venereal inspection for more than one month, and knowing that he had not been exposed to infection, the mental shock, when he was informed by the inspecting surgeon that he would be held for further observation, was more than he could endure. He fell unconscious in a convulsion not unlike that of an epileptic seizure.

From such an analysis of mental activity we arrive not only at the fundamental factors causing the phenomena of epilepsy, but we come also into possession of knowledge which guides us in our efforts to combat the disorder. We have seen that all muscular activity is dependent upon a motive force which we are wont to call feelings, or emotional state of mind, and that these emotional states are intensified in the face of opposition, unless other feelings of an irrelevant nature, which tend to weaken them, are entertained. Consequently, every individual must acquire the habit of a broad interest in the things of life that he may the more readily escape the unpleasantness of failure in particular undertakings.

This is a normal habit of which we have countless examples. In the teachings of most of our institutions of learning, emphasis is laid upon the necessity of a broad education in general subjects instead of intensive work in particular branches. The experience of the race in this direction is exemplified by many instinctive actions that may be observed. A mother will not allow her baby to lie neglected in a fit of crying, but by fondling and caressing helps it to overcome its intense emotional state of unpleasantness. Neither will she allow it to be teased or otherwise encouraged in unpleasant feelings. Who has not heard a mother's admonition, "Don't frighten the baby; you will scare it into fits?" Babies are given toys and playthings that they may be pleasantly occupied.

In a kindergarten the trying ordeal of keeping a child pleasantly engaged is minimized through a teacher trained in the art of leadership. It is an interesting spectacle to see how such an instructor can keep, all the morning and afternoon, many children happy at play. Each disturber who threatens the contentment of all present has his attention taken from his own particular whims by the mere suggestion of a new game, and before it can be realized, all are happy once more, singing and playing without a harsh word given or anyone spanked to start all crying. It is necessary, also, to make the common and high-school work attractive, for the young resent the least overtaxing of their mental powers. In college a student is urged to take part in athletics, so as to relieve his pent-up energies. A business man finds hobbies, golf or fishing, a side line to take his mind from the worries of his office. These are protective influences which tend to weaken emotions which tax our mental strength.

Everyone feels these needs instinctively, yet every individual is conscious of an opposite tendency in this world where alone the strongest survive. Everyone feels the need of sharpening his interests down to particular ends. This may be done within certain limits, but when carried too far, brings on abnormal nervous conditions. A child which manifests an intensive application to study, although we may marvel at its accomplishments, is considered precocious, and we are fearful that it cannot withstand such mental effort. The genius, limiting his field of activity, applies his marvellous amount of energy in accomplishing results of astounding importance. Yet society looks upon him as eccentric, or even crazy, because of his poverty of broad interests. He is abnormal because most men of his type become failures in a nervous breakdown of some form.

The nature of our emotional life, then, is largely one of habit in our attitude toward things about us. So, confronted with the necessity of making difficult adaptations, we can expect the resultant reaction to be normal only when there is present a well-rounded emotional development. When, therefore, we see manifestations of emotional poverty we should be on our guard for abnormal expressions in particular emotional stress. A form of stress not usually looked upon as emotional, because the patient may not be conscious of any particular feeling, is had in acute febrile states, in toxemias and the like. Under such conditions the life of the individual is threatened. It does not make any difference what the form of attack may be, even though it be worms or even eyestrain, the body as a living organism resents any form of infringement on its welfare. Therefore, if consciousness is impaired there may be an abnormal expression of that power of resentment. A convulsion is one of the abnormal forms.

In anesthesia we produce, by means of ether as a drug, an attack

on the life of the body as a living organism. The higher centers of the cerebrum are first exhausted and cease to function. If care is not taken to gain the patient's confidence before these centers are put out he has a well-developed emotional state of fear because of the ordeal before him. Even though the patient may come to the hospital unconscious from trauma, by forcing the ether the air passages are strongly irritated, producing a special insult against the welfare of the body, which will be resisted even though the conscious centers of the brain are not functioning. In anesthesia the muscular action, as an expression of resentment, becomes what we call the excitement stage and it continues until the motor centers are paralyzed. These are all abnormal expressions of emotions, and once exercised become easier with each repetition. If we would guard against a habitual exercise of such abnormal expressions we must not only combat disease processes but we must so govern conduct that strong emotional activity will be avoided.

The same principles are involved in the care and treatment of a patient who has a well-developed disorder of epilepsy. The scope of this article does not permit a discussion of the details of the method of application of these principles, for each case is largely a matter for individual consideration; yet there are certain general features of the work which may be mentioned.

The hopes for improvement and recovery in every particular case of epilepsy lie in the patient's ability to become pleasantly occupied. Patients of low-grade mentality, patients past middle age and those in whom the process of epilepsy is long established in mental habits firmly fixed offer only a guarded prognosis. It is with the young and with those early in the process of the disorder that we expect favorable results. So we look forward to the time when, instead of the greater percentage of those received being chronic in their affliction, we may have more enter suitable institutions when their epileptic seizures are first manifested. Many patients are also handicapped with physical disabilities which have been a hindrance to them all through their life. Such deformities often serve as the exciting force which narrows the field of their pleasurable activities. When possible these physical defects are corrected and the patient is put in an environment where he is not always made conscious of his troubles.

To afford an opportunity where patients of this kind may work and not be constantly reminded of their affliction as they are when employed at home the State of Indiana has established this farm, through the efforts of a leadership of the caliber of constructive genius. The wisdom of the undertaking is seen in the improvement of a patient after coming here. Almost without exception every such individual not only gains in physical health by taking on weight but makes decided mental improvement, with the result that his seizures become less frequent. Many patients coming in shackles

from insane hospitals, where they are considered the most objectionable and difficult to manage of all patients there, are in a short time found peaceably at work at various tasks on the farm.

The problem, however, of changing the mental attitude of the epileptic does not end in providing him with an opportunity for work in which he may become interested. A person habitually self-centered is always ready to resent anything that will oppose his particular ideas. The epileptic is such a person. He cannot be ordered to do a thing or be forced to work and be expected to do it joyfully. Because of his mental attitude and resultant seizures, which he considers as an affliction, he sets himself up as an object to be pitied, but he will not be satisfied with any sympathy which may be shown him. Sympathy he does not want, and he will not stand abuse. A plain understanding is all that is necessary to satisfy him. With this he seldom fails to respond to any suggestion honestly and pleasantly given.

Such characteristics cannot be said to be wholly abnormal, for no person can will or be forced to will to do a thing. There must be a reason or desire to do strong enough to overcome any conflicting notion. To help them to have desires to do things, to place them in surroundings that will aid in this, is the big thing to be considered in the care and treatment of the epileptic. Attendants must be made to understand this, for until they do they are more apt to rule by brawn than by brains, thus adding to the patients' affliction.

There are many patients who quickly show the results of the slightest mistreatment by becoming irritable, violent or even so emotionally wrought up that they develop a convulsive seizure. In a cottage for small children there is a boy who finds pleasure in standing up in his chair playing with the window-blind string. The attendant does not want him to do this. So he observed that he could, by scolding and slapping the child's hands, compel him to sit quietly in the chair. This he would do, but with a scowl of unpleasantness on his face which would shortly be terminated by his falling in a seizure. He observed, also, that instead of this procedure, that by dangling a string from his pocket alongside of the window blind string that the boy would take this string with delight. Now, by fondling and caressing the little fellow in a gentle manner he could place him in the chair where he would play peaceably with the string for hours without having a seizure. This is but one example of the right and wrong way of managing the epileptic. When mistreated his condition is made all the worse, but when handled with judgment and understanding his attention is easily attracted from the undesirable to the desirable by proper suggestion. Although many of these children are crippled or feeble-minded, even to the extent that they are bedfast, yet they manifest a consciousness of feelings of a marked degree. They know when they are warm and when they are dry and clean. They know when

they are hungry, and are conscious of many things which concern their individual welfare which we fail to notice. They love to be petted and are very solicitous of any attention that may be given them. In this they are not unlike any child, unless we seek to find particular emotional differences. A normal child has its likes and dislikes. A newborn baby does not find things altogether pleasant in its new surroundings. It has been used, before it was born, to sharing the warmth of its mother's body, to obtaining its food and breath through her blood. When born it must face new conditions, in that it must breathe for itself and obtain its food in a new way. Likewise it must tolerate rough, irritating clothing in order to keep warm. If there is anyone who thinks this a pleasant experience he will have that idea divorced from his mind if he will but gaze on the wailing face of the baby just born. From beginning, then, until the end of life every person is confronted with the necessity of meeting unpleasant experiences which may be made less tolerable if proper judgment is not used.

Besides the unfavorable attitude of the patient toward interests outside of his own immediate desires we have many other conditions which aggravate unpleasant emotional states. Our records show more seizures on Sunday than on any other day of the week. Everyone recognizes this as the "longest day of the week," because of inactivity. Such a time affords an opportunity for worrying about getting home or just any thing which would have no place in a mind exercised with pleasant occupation. Likewise, more seizures occur during the "long winter days" than in the summer. Long-drawn faces, as seen in the epileptic, tell the story of the producing mental attitude. It becomes a problem for serious study, then, if we may make conditions good enough that we can help them to develop a habitual smile.

In conclusion, then, we must look upon epilepsy as an abnormal muscular reaction to strong mental states. It is an abnormal expression because such muscular activity does not gain the end for which the emotional state was generated. It is unnatural, also, since it is effort undirected. The epileptic, because of his peculiar make-up, cannot avoid the dangers of too great stress as the normal man meets it, but by an emotional drive that cannot be readily checked, labors on to mental exhaustion in unconsciousness. This is not deep enough to involve the motor or life centers of the brain, so a convulsion takes place. Viewing epilepsy in this light, we are now able, in treating the disorder, to institute more rational methods than has previously been had in surgical procedure and in empirical therapy.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Note on the Presence of Meningococci in the Skin Petechiæ in Cerebrospinal Fever.—MUIR (*Jour. Royal Army Med. Corps*, London, 1919, xxxiii, 404) reports two instances in which death was preceded by cough and purulent sputum and by a petechial eruption. The smears from the petechiæ showed free and intraleukocytic Gram-negative diplococci. The same diplococcus was found in the blood but not in the cerebrospinal fluid, and there were no postmortem evidences of meningitis. The meningococcus belonged to Gordon's type II. These observations confirm the findings of others who, however, in some instances, thought the diplococcus differed from the usual meningococcus.

Epidemic Gastro-enteritis Due to Food Poisoning.—COMRIE and BIRD (*Jour. Royal Army Med. Corps*, London, 1919, xxxiii, 374) observed an epidemic of acute severe gastro-enteritis among British troops in July, 1918. There were in all about 400 affected troops. The symptoms were violent vomiting, frequent diarrhea, fever often to 102° F., subsiding to normal in three days. The stools were thin and bright green. Signs of circulatory failure were common in the severe cases. The epidemic was due to the use of warmed-over meat in "sea pies." In the fatal cases the *Bacillus aertrycke* (mutton strain) was found in the spleen. The same organism was found in the feces of six other cases. Treatment consisted in early catharsis followed by sedatives and cardiac stimulants. Saline infusions were tried in the very ill patients. A complete bacteriological and immunological study of the organism is presented.

SURGERY

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Treatment of Chronic Empyema.—TINKER and WATTENBERG (*Ann. Surg.*, 1919, lxx, 545) outline the results of their treatment of 80 cases of chronic empyema in the U. S. G. H. No. 26, at Fort Des Moines, Iowa. All but six of the cases had been operated on prior to their admission to the hospital. Seventy-two (90 per cent.) of their cases showed discharging sinuses from their pleural cavities. The remaining 8 cases had external wounds which had healed, but needed further treatment to develop their lung capacity and general physique. Of these 8 cases 3 reopened spontaneously soon after their admission. The majority of their cases of empyema followed influenzal pneumonia. Sixty cases had had only one rib resected, and they believe that the removal of more than one rib for drainage purposes is contra-indicated. The seventh or eighth rib was most commonly removed, the incision being made in the posterior axillary or midinfrascapular line. Of these 80 cases the length of time during which suppuration had existed prior to admission varied from twelve months to three weeks, with an average of four months. Forty of their cases were treated by the Carrel-Dakin method. The average time required for healing under this treatment was thirty-four days. Patients operated on from the eighth to the tenth day following the diagnosis of empyema progressed most rapidly. In no case did simple aspiration cure or even improve the condition. The Dakin irrigation was carried out routinely by a thorough flushing out of the whole cavity, once a day, with a liberal irrigation once every two hours. The tubes were so managed as to flush the entire cavity. In those cases which proved intractable to treatment bismuth paste was injected, hot, to fill the entire cavity, and the drainage tubes were permanently withdrawn. But 3 mild cases of bismuth-poisoning were observed in the 40 cases so treated. In addition to the local treatment, lung expansion was promoted by the use of Wolfe's bottles and by properly graduated outdoor setting-up exercises. It is believed that these results obtained from Dakin's treatment supplemented by bismuth paste when necessary, and aided by lung expansion exercises, setting up drills and a forced diet, show that a radical reoperation is unnecessary to effect a cure in the great majority of cases of chronic empyema.

Spontaneous Rupture of a Varicocele.—VAN DEN BRANDEN (*Arch. méd. Belges*, 1919, lxxii, 683) reports a case of spontaneous rupture of a varicocele which is a rare condition. Palet has compiled five cases, all occurring in old men. Van den Branden's case occurred in a young man

who experienced excruciating pain in the scrotum and fainted while shaving. Examination in the hospital disclosed an enlarged, tense scrotum. There was no history or evidence of venereal disease, but eight years previously the patient had been treated for an acute varicocele. Operation two days after admission revealed a hematocele, which was evacuated and drained. The wound healed by primary intention and the patient was discharged.

Personal Experience in the Use of Lane Plates.—SWEET (*Jour. Orthop. Surg.*, 1919, i, 673) reports 1560 fractures of long bones, with 172 open operations. Of these 41 were compound and 129 were cases of simple fractures, delayed or non-union, or were cases of vicious union. Lane plates were applied in 28 instances (femur 18, tibia and fibula 7, radius and ulna 3). Primary union occurred in all except 2 cases, and these were compound fractures. In 4 cases sinuses developed at the end of six to ten weeks, the process being afebrile. In 1 case in which the plates and screws were handled by the operator a low-grade osteomyelitis resulted. Sweet thinks operation is safer in the femur than in the other long bones, and considers operation highly satisfactory.

PEDIATRICS

UNDER THE CHARGE OF

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The Antiscorbutic Value of the Banana.—LEWIS (*Jour. Biol. Chemistry*, November, 1919) says that as a result of experiments he found that guinea-pigs fed an exclusive diet of banana were unable to maintain their bodily weight and died in from twenty to thirty days. He found in autopsy a condition of marked inanition, but no lesion characteristic of scurvy. Bananas in amounts greater than 25 grams a day as a supplement to a diet of rolled oats prevented the onset of scurvy. Such a diet did not permit normal growth in young animals. Less than 25 grams of bananas a day as a supplement to the oat diet did not protect against scurvy. Scurvy can be readily produced experimentally on a diet of autoclaved rolled oats supplemented by bran, milk casein and inorganic salts. When such a diet is supplemented by banana from 10 to 15 grams will serve to protect against scurvy, but result in rapid growth of young guinea-pigs. These experiments suggested that a lower content of the antiscorbutic principle may be sufficient to protect against scurvy, if the diet is adequate in its content of the other essential dietary constituents.

The Heat Coagulation of Milk.—SOMMER and HART (*Jour. Biol. Chemistry*, November, 1919) say that the chief factor in the heat coagulation of milk is the composition of the milk salts. Apparently casein

requires a definite optimum calcium content for its maximum stability. The calcium content of casein is largely controlled by the magnesium citrates and phosphates present. In fresh milk there is no relation between titratable acidity and heat coagulation. Acid fermentation in milk lowers the coagulability point by changing the reaction and by lowering the citric acid content. The titratable acidity of fresh milk samples varies so widely that it is impossible to determine the extent of acid fermentation by titration; so that it is impossible to use the acidity of milk as a criterion of coagulability. Difference in concentration accounts partly for the difference in coagulation of fresh milk samples. Hydrogen ion concentration is not the determining factor in fresh milk coagulation. It is nevertheless a factor in fresh milks and in commercial milk it may become an important factor.

The von Pirquet Test.—FRIEDMAN (*Colorado Medicine*, October, 1919) publishes the results of observations on 464 unselected patients. Their ages ranged from a few months to eighteen years. Of this number 219 were males and 245 were females. Of these 39.8 per cent. reacted positively, the number of positives among the males being 2 per cent. in excess to that found in the females. Under one year almost 12 per cent. reacted positively; from ten to fourteen years, 55 per cent.; and from fourteen to eighteen years, only 51 per cent. The highest number of positive reactions was noted during the eleventh to thirteenth year period, with 66.7 per cent.; and the lowest at the fifth to the sixth year period, with only 13 per cent. positive. Of 27 having a tuberculous parent 23.2 per cent. reacted. Of 181 children exposed to a parent with an active lesion 58 per cent. reacted positively, and of 78 cases exposed to a parent with a healed lesion, 38.5 per cent. reacted positively. Of those children whose father had a healed lesion, 48.4 per cent. reacted positively. Of 210 children examined from eighty-five families all members of the same family reacted positively in 55 instances. One hundred and eleven tests were performed upon 55 children at intervals of from several months to two and a half years. In 43 the outcome was the same with both tests. In 11 a negative result became in a subsequent test positive, and only once did a positive test become negative. In 6 children the first positive test was more pronounced, in 7 the second was more pronounced. In this series only 5 were found in whom clinical tuberculosis was demonstrable; 4 showed apical involvement and 1 has tuberculosis of the spine. None of these was under fourteen years of age; 4 were of tuberculous parentage; 3 reacted positively, but only 1 of these showed a strong reaction.

The Nervous Child and His Management.—McCREADY (*Jour. Am. Med. Assn.*, October 11, 1919) points out some of the factors giving rise to the development of nervous disorders of later life. As regards treatment he suggests that this must begin with the modification of the immediate environment. The difficulty of improving in his own home is not because the home is essentially unfit but because it is difficult to eliminate the causes of the nervous disorder. Because of lack of special training the parents and relatives should be out of contact with the little patient. If the child is kept at home the domestic arrangements must be modified and changed as conditions require, sources of friction

must be removed, impatience, irritability and undue sympathy must be eliminated. Rest is the first essential. Next comes regulation of diet. Excessive carbohydrate consumption in the form of candy and pastry are to be eliminated. Fresh air, bathing, regulated exercise all have an important place in the hygienic management of the nervous child.

OBSTETRICS

UNDER THE CHARGE OF

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Transmission of Smallpox to the Fetus.—CAPPELANI (*Pedriatia*, Naples, April, 1919) observed four cases in which the newborn infants developed smallpox immediately after birth. At first these children seemed normal, but in five or six days smallpox developed. In one the mother was healthy but the infant had fever twenty-four hours after birth and developed smallpox the next day. The mother was revaccinated at once giving a typical response, but escaping smallpox, although the disease was prevalent at the time.

Cesarean Section for Hemorrhage from Varicose Veins of the Vagina.—BRUNNER (*Correspondenzblatt f. Schweiz Aerzte.*, March 15, 1919) has collected cases to show that hemorrhage from varices in the vagina during pregnancy is often fatal. In one collection of 15 cases there were 13 deaths, and during labor in a series of 16 cases there were 7 deaths. Another observer in 30 cases found 11 deaths and another in 3 cases had 2 deaths. In 1 case the obstetrician was able to arrest the bleeding by tamponing, but the moment the tampon was removed the blood spurted anew from various points. He delivered the patient by abdominal Cesarean section and the varices by the third day had collapsed. Brunner reports a case in which the child was very large, weighing 4900 grams. Profuse and persistent bleeding came on during labor and the labia were so edematous that ligatures would not hold and the hemorrhage was controlled by clamps. After abdominal section the woman recovered and her recovery was complicated by sepsis for which she received antistreptococcus serum.

Drugs Contra-indicated During Pregnancy.—MUNOS (*Repertario de Medicina y Cirugia*, Bogota, February, 1919) would not administer potassium iodid to pregnant women. He asserts that he has seen it induce abortion, killing the fetus in later pregnancy and even disturbed nursing infants when the drug had been applied externally to the breasts. Iodin acts comparatively like a stimulant with menstruation. Russian physicians have been in the habit of using iodine and potassium iodid extensively in typhus fever. In amenorrhea in robust

women iodide is useful and in the neuralgias of diabetics hypodermic injections of solution of potassium iodid often do good. These injections take the place of morphin. In albuminuria and nephritis morphin must be avoided.

GYNECOLOGY

UNDER THE CHARGE OF

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Large Doses of Radium in Cancer.—TURNER (*Lancet*, 1919, cxvii, 1018) is of the belief that in treating cancer of the cervix with radium it is important to give at first a sufficiently large dose and he is accustomed to administer from 5 to 10 and even 15 thousand milligram hours and he states that he has never seen bad results follow such large doses. Suppose that the amount of radium employed in a particular case amounted to 100 mg., which is commonly the case, then a dose of 10,000 mg. hours would be administered by keeping it *in situ* for 100 hours. It might be suggested that it would be well to divide the exposure into two or more parts at intervals of a week or two, but Turner states that this will not answer and the whole dose should, if possible, be given at once. The patient should be kept in bed for a short period after exposure and should be douched. She may then return home but should report herself in about three months if all be going well, by which time it is possible that all the local evidences of the disease will have disappeared. Such dosage as Turner recommends is considerably in excess of the average dose of the American gynecologist for similar cases and it is very encouraging to note that such large doses can be given without causing extensive destruction of the surrounding tissues.

New Method of Uterine Suspension.—The permanent operative correction of a well marked uterine prolapse has always been one of the bugbears of gynecological surgery and therefore a new method of treatment which utilizes a strip of fascia lata, suggested by FREEMAN (*Surg., Gynec. and Obst.*, 1919, xxix, 511), may be of interest to those who have to treat such distressing conditions. Having obtained access to the abdominal cavity through a median suprapubic incision of sufficient size, the uterus is brought up into the opening and inspected. If the patient is still within the childbearing period, she must be sterilized, best by ligation of the tubes with silk, dividing them and perhaps folding the severed ends upon themselves. A strip of fascia lata, about six inches in length and three-fourths inch in width, is then obtained from the outer side of one of the thighs in the following manner: An incision of sufficient length is made through the skin and subcutaneous fat directly

down to but not through the glistening white fascia, and extending along the lateral aspect of the limb, midway between the trochanter and the knee. With a gauze covered finger the adipose tissue is pushed to either side so as to clear the field and the fascia divided in two parallel lines of the required length. The strip is then loosened and elevated by slipping the handle of a scalpel beneath it and sweeping the instrument from one end to the other. After dividing the attached ends with scissors the strip is removed and enveloped in moist gauze until required. The slit in the fascia lata from which the graft was taken may then be closed with a running suture of chromic gut, although this is not absolutely necessary because no harm will result if this is not done. Returning to the abdomen, the uterus is held firmly while a pair of small, sharp pointed, curved hemostatic forceps is plunged from one side to the other directly through the substance of the uterus close beneath the peritoneum covering the fundus, but not penetrating into the cavity. The forceps should be entered just internal to the attachment of one of the tubes and brought out at a corresponding point upon the opposite side, although if the organ is large it may be well to tunnel it somewhat more anteriorly in order to prevent undue pressure upon the bladder when the uterus is suspended from the tendons of the recti muscles. In order to facilitate the insertion of the forceps, it is occasionally desirable to nick the peritoneum with the point of a knife. When the forceps have been passed and are still in position, the fascia is doubled longitudinally upon itself, one end seized in the jaws of the instrument and the strip dragged through so that its center rests in the middle of the tunnel and its loose ends project from either side. Catgut stitches are then inserted so as to close the openings of the tunnel, thus preventing oozing and holding the fascia in place. The next step is to secure the ends of the fascia around the tendinous insertions of the recti muscles in order to bind the fundus of the uterus securely and closely to the anterior abdominal wall. This is accomplished first by stripping back the anterior sheaths of the muscles for a short distance above the pubes, so as to uncover the tendons, and plunging through these and the underlying peritoneum from without inward, a pair of pointed hemostatic forceps with which the ends of the fascial strip are seized and dragged into place, one on either side of the abdominal incision. After the peritoneum is closed, the ends of the fascial strip, which have been retained in forceps to prevent retraction, are pulled tight enough to hold the uterus firmly against the abdominal wall and are then crossed over the median line, best by tying them in a half-knot, and stitched securely to each other in several places by means of chromic gut so that they cannot slip. The wound is then closed in layers. Additional security against slipping may be obtained by catching the ends of the suspending fascia in the bight of a figure-of-eight silkworm-gut suture used in closing the abdominal incision. Fascia lata has a number of things in its favor: (1) It is easy to obtain in any desired quantity. (2) It is very strong and will not stretch to an appreciable extent, thus differing from the natural supporting ligaments of the uterus. (3) It does not become absorbed, like catgut, but incorporates itself within the tissues and permanently holds the uterus where it is placed.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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A Comparison of Certain Antigens used in Complement-fixation Tests in Pulmonary Tuberculosis.—YOUNG and GIVLER (*Am. Rev. Tbc.*, 1919, iii, 476) compared the value of three antigens, the Petroff methyl alcohol soluble, the Corper autolysate and the Wilson bacillary. Their purpose was to find if the Wilson antigen was more suitable for complement-fixation tests than the others. This did not prove to be the case. Examining known cases of tuberculosis, they obtained best results with the Petroff antigen, obtaining 66 per cent. positives against 63 per cent. with Corper antigen and 57 per cent. with the Wilson antigen. They felt there was no justification for the use of the Wilson antigen, the bacilli emulsion having lost much of its antigenic properties by the alcoholic extraction in the preparation. They showed that when this extraction was carried further all of the antigenic properties are destroyed. They found the human hemolytic system superior to the sheep system in doing the tests. The serum of only 12 out of 75 guinea-pigs used proved unsuitable.

Toxic Necrosis and Regeneration of the Acinar Cells of the Pancreas.—Heretofore our knowledge of the action of various toxins upon the acinar cells of the pancreas with the occurrence of mitotic figures and evidences of regeneration has been quite meager. PARKER (*Jour. Med. Res.*, 1919, xl, 471) studied sections from some four hundred autopsies, of which one hundred showed lesions of necrosis in the acinar cells of the pancreas. All tissues were fixed in Zenker's fluid and stained by Mallory's eosin-methylene blue method. The author classifies the necroses of the pancreas etiologically into (1) acute pancreatitis with fat necrosis; (2) necrosis due to toxins; (3) infectious pancreatitis arising by direct extension along the ducts, from the blood stream or from a neighboring focus. In toxic necrosis the pancreas, macroscopically, shows no changes. Microscopically, necrosis may occur in a single acinar cell, groups of cells or diffusely, the total number varying considerably. As in other organs, the necrotic cells are quickly removed by polymorphonuclear and endothelial leukocytes, regeneration rapidly ensues and repair is complete. Inasmuch as similar lesions were found in the heart, liver, kidney and adrenals, because of the type of associated infection, by the fact that there was no involvement of the stroma and no demonstrable organisms, it is concluded that the necroses are of toxic origin. The necroses were most frequently encountered in pneumonia, diphtheria, acute peritonitis and other suppurative processes, due to streptococcus or pneumococcus. In a study of eighty-five cases it was found that the adrenals, pancreas, liver, kidney and heart showed toxic lesions most frequently in the

order named. Experimentally, a guinea-pig was subjected to chloroform vapor for two hours. Autopsy material showed active regeneration of liver, adrenal and pancreas, the latter exhibiting no remains of necrotic cells. Another guinea-pig was given liquor potassii arsenitis by mouth and died in five days. Sections showed fatty degeneration of the liver, but no necroses or mitoses, while the pancreas, kidney and particularly the adrenal showed no necroses but signs of active regeneration. The author concludes that these experiments confirm the findings in the human cases in that substances affecting the liver, kidney and adrenal affect the pancreas.

Studies in Epidemic Encephalitis.—LOEWE, HIRSHFELD and STRAUSS (*Jour. Infect. Dis.*, 1919, xxv, 378) report results of injection of monkeys, subdurally and rabbits intracranially, with filtrates of nasopharyngeal mucous membrane from cases of epidemic encephalitis. Lesions were produced in monkeys and rabbits similar to those found in the human brain in fatal cases of epidemic encephalitis. The virus was carried through four generations in rabbits, transmitted to a monkey in the fifth generation and then brought back to rabbits. A natural immunity was found in 50 per cent. of the rabbits. The virus was recovered from the nasopharynx of an animal inoculated intravenously. Cultures of the material used for inoculation were negative.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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An Investigation of the Shaving Brush Industry, with Special Reference to Anthrax.—The Public Health Service (*Public Health Reports*, 1919, xxxiv, 994) makes a report on the shaving brush industry from the anthrax viewpoint, as a number of cases of facial anthrax have occurred from contaminated brushes. It appears that the anthrax spores are found almost exclusively on horse-hair imported from oriental sources, and various more or less efficient means of treating the hair were in use, but it was found that boiling or steaming of the hair offered the best means of destroying anthrax spores.

Fishes in Relation to Mosquito Control in Ponds.—HILDEBRAND (*Public Health Reports*, 1919, xxxiv, 1113), an ichthyologist of the U. S. Bureau of Fisheries, reports on the efficiency of top minnows, *Gambusia*

affinis, in the destruction of mosquito larvæ, with the object of aiding antimalarial work. The particular fish selected has the advantage of not requiring special environment for depositing eggs and hatching, as the young are borne well developed and will begin to destroy larvæ when only a day old. The top minnow must be protected from man, who uses them for bait, and from certain predatory fishes, notably black bass. Overgrowth of vegetation furnishes a natural protection for *Anopheles* larvæ which prevents the top minnows from reaching them. The author saw one top minnow eat 165 larvæ in less than twelve hours. The number of minnows required varies with local conditions; it is not possible to have too many. The author considers these fish valuable aids in antimosquito work and points out their limitations.

The Nature of Contaminations of Biological Products.—BENGTSON (*Hygienic Laboratory Bulletin No. 112*, U. S. Public Health Service, Washington, D. C.) found that the contaminations that occur accidentally in biological products were in general harmless for laboratory animals. Cocci and both spore-bearing and non-spore-bearing rods were present. An organism resembling the tetanus bacillus was found, but was without pathologic effects. Pathogenic contaminations are believed to be of animal origin and are chiefly found in products from animal sources while bacterial vaccines all proved to be contaminated with saprophytic forms.

Phenols as Preservatives of Antipneumococcic Serum. A **Pharmacological Study.**—VOEGLIN (*Hygienic Laboratory Bulletin No. 112*, U. S. Public Health Service, Washington, D. C.) studied the effects of the administration intravenously to animals of mixtures of horse serum and phenol and trikresol, using doses that would contribute evidence as to the possibly deleterious action of the preservatives when the preserved serum is used in the treatment of pneumonia. The observations were made on normal animals and on those suffering from pneumonia. It was shown that certain toxic manifestations were less pronounced when a phenol-serum mixture was used than when the same amount of phenol was given in Ringer's or Locke's solution. The worker shows that phenol and trikresol may safely be used as preservatives of serums that are given in even such large doses as is the case with antipneumococcus serum and that the injections should be made at a slow rate.

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ORIGINAL ARTICLES

CARCINOMA OF THE DUODENUM.

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CARCINOMA of the duodenum is of sufficiently rare occurrence to warrant the recording of cases.

The patient whose history follows was admitted to the University Hospital June 12, 1919:

M. O., aged sixty-three years; white; male.

Chief Complaint. Pain in the right side of the abdomen.

History of Present Illness. About five months ago he first noticed pain in the right upper abdomen, coming on just after meals, and usually worse at night. He was nauseated at such times and belched gas very freely and frequently, but never vomited and has never been jaundiced. For over a year he has been distended after meals and has belched gas quite freely, with relief; he had no actual pain until five months ago. Since onset he has lost thirty-four pounds. Pain has been practically constant ever since onset, recently radiating to the back, and becoming steadily more and more severe. Eating seems to relieve the pain for a short time. No genito-urinary symptoms.

Previous medical history, social history and family history negative.

Physical Examination. Adult male, apparently about seventy years of age, poorly nourished and underdeveloped. He complains at intervals of severe pain in the right hypochondrium, radiating to the back, but at other times is apparently quite comfortable. Skin is rather swarthy; no jaundice; no cyanosis; no eruptions.

Blood-pressure. 143 to 47.

Head. Well-formed, with no gross abnormalities. Temporals are fairly hard but not nodular or tortuous.

Eyes. No congestion. Pupils well contracted, responding promptly to light and in accommodation, equal and regular; no nystagmus; no extraocular palsies. Both lenses are apparently partly opaque, and the left one shows a distinct black streak on examination by the ophthalmoscope. Eye-grounds are dimly seen but appear to be of good color, with prominent and glistening arteries; no hemorrhages; no exudates.

Nose. Moderate deflection of the septum to the right; no obstruction.

Ears. Negative.

Mouth. Lips moist and of good color. Teeth in very bad condition. Many are gone, and those remaining are discolored and show plenty of pyorrhea. Tongue is broad and moist, with a heavy white coat; protrudes normally. Pharynx is moderately congested, with a thick coating of mucus. Tonsils are not visible.

Neck. No adenopathy; no abnormal pulsations; no tracheal tug; no thyroid enlargement.

Chest. Rather poorly formed, with fair expansion, equal and regular throughout. Resonance, fremitus and voice and breath sounds are physiological. No rales or frictions.

Heart. R. B., 2.5 cm.; R. O., 9; L. B., 10.5 cm.; L. O., 13 cm.; height, 7 cm. Apex-beat not visible or palpable. Sounds very distant and of poor muscular tone; no undue accentuation; no murmurs. There is an occasional tendency to bigeminate rhythm, with the second of the sounds louder than the first, probably ventricular extrasystoles. No other arrhythmia.

Abdomen. Scaphoid. Distinct cardiac pulsation in the epigastrium. Left side is not tender or rigid and the spleen is not palpable. Right rectus is rigid throughout, more so in upper third, which is also very tender to palpation. There is fulness in the epigastrium that suggests a firm, fixed mass below. Liver is not palpable. Left inguinal canal is weak at lower third and gives impulse on coughing, and when not restrained a hernia protrudes there. Left external ring also patulous and gives impulse on coughing. Right side apparently normal. No adenopathy.

Extremities. Poorly muscled. No paralysis; no sensory abnormality. Reflexes normally present throughout. No Kernig; no Babinski; no clonus. Moderate radial sclerosis. No tortuosity. No nodules.

July 21. Urine: Light amber; cloudy; flocculent sediment; specific gravity, 1.026; acid reaction; albumin, 0; sugar, 0.

Microscope shows: Casts, 0; cylindroids, 0; mucus, +++; red blood cells, 0; white blood cells, 1 to 2; epithelium, +; crystals, 0.

Blood Wassermann, negative.

July 25. *Gastric Contents*. Quantity, 100 c.c.; normal odor; white color; total acidity, 94; free HCl, 64; occult blood, 0. Starch, +++; yeast, +; fat, ++; other food masses, 0; occasional epithelium; mucus, +; Oppler-Boas and sarcinae, 0.

Gastro-intestinal Roentgen-ray Report. Stomach: Adhesions or possible ulcer near pylorus. Duodenum: Probably negative. Colon: Fair position. Marked stasis. Exquisite tenderness always over right iliac fossa region, cause not determined.

July 26. Phenolphthalein elimination—intravenous: First hour, 50 per cent.; second hour, 10 per cent.; total, two hours, 60 per cent.

Blood-urea nitrogen, 18 mg. per 100 c.c.

Blood: Red blood cells, 4,700,000; white blood cells, 9800; hemoglobin, 70 per cent.

Differential: Neutrophiles, 68 per cent.; lymphocytes, 24 per cent.; large mononuclears, 4 per cent.; transitionals, 4 per cent.; eosinophiles, 0 per cent.; basophiles, 1 per cent.

Tentative Diagnosis: Carcinoma ventriculi.

August 11. Operation: Right rectus incision; stomach enlarged and somewhat ptosed. There was a sheet of "pathological peritoneum" stretching across the duodenum to the edge of the liver, which was seen by the roentgen rays, obstructing a view of the gall-bladder. The first part of the duodenum was markedly dilated. The "pathological peritoneum" was separated and the gall-bladder was found to be apparently normal except for a slight dilatation. The marked dilatation of the duodenum was the outstanding feature. Palpation of the duodenum disclosed a hard, irregular mass on its inner posterior wall near the termination of the second portion. The duodenum was mobilized. It was then opened and the ulcerated carcinomatous mass was found to originate below the papilla of Vater. It had invaded the head of the pancreas to such an extent as to make the point of differentiation impossible. A section was taken out for diagnostic purposes and the duodenum closed. A posterior gastro-enterostomy was then performed and the abdomen closed without drainage.

August 11. The patient reacted well from the operation.

August 12. Feels well. Some pain. Peristalsis started. Given albumen.

August 13. At 6.40 A.M. patient suddenly had leaky skin. Shock. Pulse absent at wrist. Heart dilated both ways. Skin pale and leaky. Given atropin because of beginning pulmonary edema. Given digalin and camphorated oil, minims xv each. Condition unimproved and patient died of cardiac failure at 8.40 A.M.

Pathological Report. Dr. Weidman. Duodenal carcinoma.

Frozen section shows complete loss of surface epithelium, the base consisting of a mass of nondescript material which gives way more deeply to a more or less devitalized fibrous tissue heavily infiltrated with lymphocytes and plasma cells. Still deeper the fibrous tissue becomes looser, more cellular, and in the very deepest parts of this fibrous layer shows acini of a cancerous type—that is, they are irregular in distribution and shape and have a rather active proliferating type of epithelium. In one or two instances such acini abut directly upon the muscular tunic, and selected places can be seen extending between the bands into comparatively deep positions. The invasion in the section

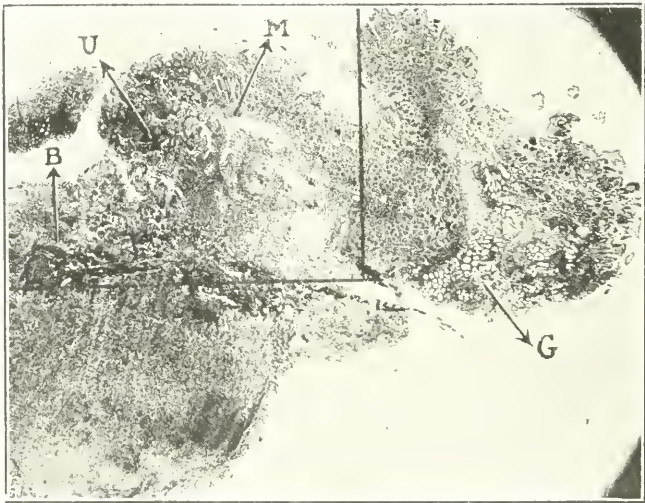


FIG. 1.—Low-power view of margin of ulcerated area. The more normal duodenal mucosa at extreme right, showing Brunner's glands at *G* and muscularis mucosa at *M*. Margin of ulcer at *U*, where the carcinomatous change is developed. Base at *B*. The upper left-hand rectangle is shown in higher magnification in Fig. 2.

studied cannot be definitely traced from the surface epithelium, and the type of acinus leads one to the opinion that it does not extend from such, but rather from a more alveolar type of glands, such as the pancreas or Brunner's glands. The muscle fibers in the external coats show granular cytoplasm and some shrinkage of nuclei, indicating a devitalized condition well short of necrosis.

Additional sections prepared by the paraffin method show an undoubted carcinoma of adeno type. Furthermore, it is perfectly clear that the tumor has sprung from the surface of the duodenum and not from Brunner's glands or the pancreas.

Postmortem Examination. A complete postmortem was not

obtainable, so an inspection was made through the original operative incision. The operative site was in excellent condition.

At the terminal end of the second portion of the duodenum was a grayish, ulcerated, indurated mass, approximately 2.5 cm. square, which was continuous with two distinct indurated masses about 2 cm. in diameter in the head of the pancreas.

There was no obstruction of the common bile duct, nor evidence of obstruction of the pancreatic ducts, nor other evidence of metastasis.



FIG. 2.—High-power view of Fig. 1. Transition from the more normal to the neoplastic is occurring in the darkly stained region at C. Compare with Fig. 1.

Notes on the Clinical Aspect of the Case. It is probable that this case is one of primary duodenal carcinoma, although the history is very similar to that of ulcer. The rapid loss of weight and the rather short duration of the disease, on the other hand, would point to primary carcinoma. It is remarkable that with such extensive involvement the patient should not have had any vomiting.

The duration of life in primary duodenal carcinoma varies according to various writers Fenwick gives seven months as an average while Pic gives from three months to a year.

Frequency of Carcinoma of the Duodenum. Primary carcinoma of the duodenum is a very rare disease. According to the reports of the Mayo Clinic only 3 per cent. of carcinomas of the entire intestinal tract originate in the small intestine. Of 3563 cases of malignant tumors of the intestine, Brill found only 2.5 per cent. in the small intestine, while Jefferson in 4177 collected cases of intestinal carcinoma finds 3.1 per cent. to be duodenal.

The following tables will give an idea of the relative frequency

of duodenal carcinoma and its relation to carcinoma in other parts of the small intestine:

TABLE I.

Author.	Source.	Total autopsies.	Duodenal carcinoma.
Schleringer	Vienna	42,000	7
Nothnagel	Pathologic Institute, Vienna	21,358	5
McGlinn	Philadelphia General Hospital	9,000	1
Rüpp	Zürich	4,258	1
Fr. Müller	Basle, 1874-1904	11,314	6
Fenwick	London Hospital	19,518	18
M. Müller	Berne, 1886-1891	5,621	6
Perry and Shaw . .	Guy's Hospital	17,652	4
Maydl	Wiener Allgemeines Krankenhaus	20,480	2
		151,201	50

Average incidence of carcinoma of the duodenum, 0.033 per cent.

TABLE II.

Author.	Duodenal carcinoma.	Jejuno-ileal carcinoma.
Köhler	9	3
Mayo	5	17
Nothnagel	7	11
M. Müller	6	3
Rüpp	1	1
Barnard	5	10
Lubarsch	2	2
Fr. Müller	6	2
Maydl	2	4
Schlieps	20	16
	63	69

Average of duodenal carcinomas, 47.7 per cent.

Average of jejuno-ileo carcinomas, 52.2 per cent.

Of 343 cases of intestinal carcinoma collected by Nothnagel at the Pathological Institute between 1870 and 1893, 7 were in the duodenum and 11 in the ileum; and of 542 cases collected by Schlieps, 20 were in the duodenum and 16 in the ileum; while the Mayo Clinic, in 1846 cases of carcinoma of the intestine, finds the duodenum involved in 5 cases and the ileum 6, and the jejunum 11 times.

Situation and Relative Frequency at Various Sites of Duodenal Carcinoma. Pic's topographical classification is as follows:

1. Parapyloric.
2. Peri-ampullary.
3. Perijejunal.

Ewing classifies them as:

1. Carcinoma following ulcer.
2. Carcinoma at the papilla of Vater.
3. Carcinoma of the third portion of the duodenum.

While the Mayo Clinic classifies them as:

1. Supra-ampullary.
2. Ampullary.
3. Infra-ampullary.

TABLE III.

Author.	First part duodenal.	Second part.	Third part.
Mayo	5 ¹		
Rolleston	8	24	3
Geiser	11	51	9
Fenwick	11	29	7
	—	—	—
	35	104	19
Percentage	22.15	65.82	12.02

These statistics seem to show that taking the small intestine into account, inch for inch, the first portion of the duodenum is more likely to undergo malignant degeneration than other portions of the small intestine, and in the duodenum *per se* we find that the second portion is much more liable to undergo malignant change than is the first or third portion. This is undoubtedly due to the presence of the ampulla of Vater and the occasional separate opening of the pancreatic ducts. The incidence of carcinoma of the first portion of the duodenum, on the other hand, may be due to the fact that this is the favorite site of duodenal ulcer. How frequently carcinoma of the duodenum is engrafted upon a chronic duodenal ulcer is, of course, uncertain. One thing is certain, that carcinomatous degeneration is not nearly so frequent in duodenal as in gastric ulcer.

Letulle, Perry and Shaw and Nathan-Larrier have reported 10 cases while Jefferson has collected 20 more, making a total of 30 cases in the literature in which evidence was found that duodenal ulcers had undergone malignant change. The location of these tumors chiefly near the pylorus agrees with the statistics as to the site of chronic duodenal ulcers; Collins in 262 cases reports 242 cases of involvement of the first portion and 14 of the second.

Pathology. 1. Carcinoma following duodenal ulcer differs little from that of pyloric ulcerocarcinoma. The lumen of the duodenum is nearly always encroached upon. There is a tendency to early metastasis. The stomach is frequently greatly dilated. It is likely that many of the so-called pyloric carcinomas which are operated upon, probably arise from the duodenum and extend into the pylorus.

2. Carcinoma of the second portion most frequently arises in or about the papilla of Vater. Jaundice is a very constant and persistent symptom, although it is not so severe as in carcinoma of the ampulla. There is frequently a dilatation of the biliary and pancreatic ducts, with the formation of pancreatic retention cysts. Krause, Jefferson, Gerster and Geiser have also observed fat necrosis in these cases. The structure is commonly that of a cylindrical-celled adenocarcinoma. Frequently the tumors, as in

¹ Several of these cases also involved the papilla of Vater.

the case described, are very closely associated with a mass in the pancreas, while occasionally microscopically a duodenal carcinoma resembles pancreatic tissue and not the cells of the cylindrical variety, so that an origin from pancreatic rests has been suggested. Branham has reported one such case. Others have noted the presence of Brunner's glands in these growths. A case of this type has been reported by Orth.

3. Carcinoma of the third portion, as our Table III shows, is the most infrequent of all carcinomas of the small intestine. Most of these take the form of a broad, flat, ulcerating mass, with stenosis. There is dilatation of the first and second portion of the duodenum. The structure is usually a cylindrical-celled or an alveolar carcinoma.

Diagnosis. If a tumor is palpable it is not easy to distinguish it from a tumor of the pylorus. Tumors of the second or third portion are usually fixed while those of the pylorus or first portion of the duodenum are movable.

Pyloric tumors are usually associated with more marked symptoms of gastric obstruction and dilatation, except in the high cases of the first portion of the duodenum. Jaundice points to carcinoma of the duodenum, as does a normal acidity of the gastric contents, while in carcinoma of the stomach dyspeptic symptoms occur earlier and are more serious.

Tumors of the second portion, especially the papillary ones, may prove fatal by biliary obstruction and severe infection. These cases may terminate by sudden single or repeated hemorrhages.

In cases associated with obstruction of the pancreatic ducts, Einhorn called attention to pancreatic diarrhea, the patient having copious, fatty, pale and offensive stools containing recognizable portions of undigested food.

In tumors of the third portion gastric symptoms with vomiting of great quantities of biliary material are prominent.

SUMMARY. 1. Carcinoma of the duodenum is a rare condition. It is found in 0.033 per cent. of hospital autopsies.

2. The percentage of carcinomas of the entire intestinal tract originating in the small intestine varies from 2.5 per cent. to 3.1 per cent.

3. The relative proportion between carcinoma of the duodenum to that of the jejunum and ileum is 47.7 per cent. to 52.2 per cent.

4. Inch for inch the duodenum is much more liable to undergo carcinomatous change than the jejunum or ileum.

5. The relative frequency at various sites of duodenal carcinoma is as follows: First portion, 22.15 per cent.; second portion, 65.82 per cent.; third portion, 12.02 per cent.

6. Carcinomatous degeneration of chronic duodenal ulcers is not nearly so frequent as in chronic gastric ulcers.

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NUTRITION AND PUBLIC HEALTH WITH SPECIAL REFERENCE TO VITAMINES.¹

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NOTWITHSTANDING the fact that my first biological interest was in relation to the subject of nutrition, my earlier experiments were made on myself and were discontinued as soon as my curiosity was satisfied, and I have had occasion to work out, in a scientific manner, only small details of this vast subject. While serving with the Division of Food and Nutrition, Medical Department, U. S. Army, I was impressed with the wide differences of opinion that exist in

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the public mind, and especially among the medical profession, on this subject, and since January 1, 1919, with the assistance of ten students, I have devoted nearly all of my time to investigation in this field, the results of which are being published in the *Journal of Biological Chemistry*. Owing to the fact that the changed economic conditions due to the war have brought about some changes in dietary habits, the effects of which may not be thoroughly appreciated until some years have passed, a compilation of some of the literature and discussion of some of the problems may not be out of place at this time. Since vitamine studies are receiving considerable attention just now, attention will be directed especially to them throughout most of this paper. Other subjects will be treated more briefly, not because they are less important, but because they are better understood.

EFFECT OF FUEL VALUE OF DIET ON BODY WEIGHT. Benedict, Miles, Roth and Smith have so thoroughly investigated the effects of a restricted diet (about 2 ounces protein and 2000 calories per ration) that further comment seems unnecessary. Similar restrictions of diet have been voluntarily or involuntarily made by large numbers of persons during the war. One common conclusion from these experiments may be emphasized here, since I have heard it repeatedly denied by persons who had no reliable information on the subject, and that is that the body weight is just as much dependent on the calorific value of the food in man as in animals. Perhaps many persons partake of a low calorific diet in the presence of an abundance of food, owing to various factors that reduce the appetite. In animal experiments a diet that is inadequate in regard to some constituent reduces the appetite. This has been especially noticed in experiments in which one or more of the amino-acids or vitamins was deficient in quantity. Animals on a vitamine-free diet finally refuse food entirely. This factor may be suggested as a possible danger in so-called low protein diets.

As early as 1887, Hirschfeld advocated a low-protein diet and the same ideas have been proposed by many scientific and unscientific propagandists since that date. In 1898, while a university student, subject to compulsory physical exercise, I restricted my diet for three months in regard to the quantity of animal foods taken. My weight dropped to 70 pounds and my skin became rough, the hair on my body and face standing at right angles to the skin surface. At the end of this experiment I partook of a liberal diet, including fresh meat and vegetables, eggs, milk, beef fat, cod-liver oil, raw bone-marrow and malt extract, and at the end of one year my weight was 140 pounds, showing a gain of 3 ounces per day. In order to distinguish between quality and quantity of the diet I made another experiment in 1912. After having maintained a fairly constant weight under certain conditions for several years, and without consciously disturbing those conditions, I added about

2 ounces of cottonseed oil per day to my diet and gained 3 ounces per day for eighty days. Since the oil was drunk after meals it did not interfere directly with my appetite, and since it is not known to contain a vitamine or other growth-producing substance, it probably acted purely through its calorific value or was stored, together with water, as adipose tissue. Since fat does not cause excessive water storage, as is the case with carbohydrate, the increase of about 15 pounds in weight cannot be attributed to water storage alone.

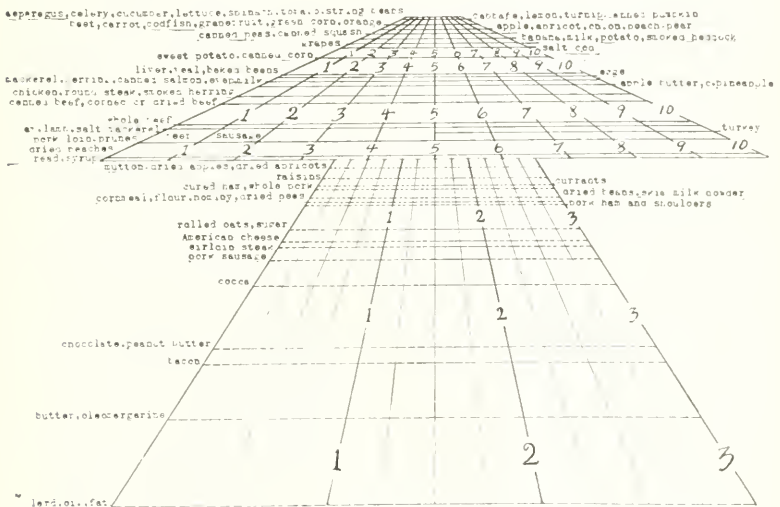


Chart for rapid calculation of fuel value of diet. The calorific value of any food may be calculated from its weight in pounds by finding the name of the food in the chart and the number corresponding to its weight on the line containing its name. Apply a millimeter tape to the scale on the chart and each millimeter represents 100 calories. In the upper part of the chart the scale reads in pounds from one to ten. In the lower part of the chart the scale reads in pounds from one to three and further divisions signify halves and quarters of a pound and the breaks in the horizontal lines signify ounces. Foods of the same calorific value are on the same line and their weights may be added together before using the chart. In order to use the chart for simultaneous multiplication and addition, prepare the list of foods in pounds and measure the pound scale of each successively with the millimeter tape, commencing each measurement on the tape at the end of the preceding one. The final figure on the tape with two ciphers added represents the total number of calories of the entire list of foods.

Although a restricted diet has been advocated by Horace Fletcher, Chittenden, and more recently by Hindhede, these propagandists seem to be in the minority. Another point of view is illustrated by the excuse a slave gave for stealing a chicken: "Nigger meat's wurf mor'n chicken meat." There are some uses of a restricted diet, however, but the difficulty lies in enforcing the dietary rules. It is said that in the treatment of obesity at Carlsbad the patients were served very small portions at high prices *à la carte*.

In economical rationing a rapid and inexpensive method of calculation of fuel value of food is desirable. By means of the chart shown, simultaneous multiplication and addition is performed in calculation of the calorific value of a list of foods. The time required is chiefly used in finding the name of the food on the chart, and hence speed increases with practice. The first time I used this chart the percentage error and the number of minutes required were carefully noted. The food used by the 9th Engineers in one week was used in the test. It required five minutes to calculate the calorific value of this food with the chart, and the error was 5 per cent. By taking more time to read the chart, or by using a chart on a larger scale, greater accuracy may be obtained in the calculation, but since the accuracy of the data may not exceed 5 per cent., greater accuracy in calculation may not be desired.

REACTION AND BACTERIOLOGY OF THE ALIMENTARY TRACT. The reaction of the alimentary tract is important in relation to the character of the hydrolysis of the food, either due to digestive juices or bacteria. The saliva in the closed mouth is about neutral. The gastric juice is about one-tenth normal hydrochloric acid and the exact hydrogen ion concentration of the stomach contents depends on that of the food and the relative quantity of gastric juice that has been secreted (as well as the degree of mixing.) McClendon and Sharp have shown that with the occasional exception of fresh milk, both raw and cooked foods are slightly acid. It should be noted that in the paper by McClendon and Sharp the first table (quoted from Clark and Lubs) should be omitted, since acid or alkali had been added to the food juices in many cases. The low acidity of the contents of the infant's stomach after feeding is not so much due to lower acidity of the gastric juice as to the diet of fresh milk, and possibly to the small quantity of gastric juice secreted. It was shown by McClendon, Myers, Culligan and Gydesen that the small intestine is slightly acid in young and adult carnivora and young herbivora. In adult herbivora, however, the duodenum is usually slightly acid, but this passes over to a slightly alkaline reaction somewhere in the small intestine. The reaction of the rabbit's intestine could be changed from alkaline to acid by flooding it with soluble carbohydrate, as by adding lactose to the diet or feeding carrots exclusively.

According to Metchnikoff the presence of acid-producing bacteria in the intestine inhibits the growth of putrefactive forms. Torrey has shown that flooding the intestine with soluble carbohydrate, especially lactose, increases the ratio of the acid-producing to the putrefactive bacteria. This is in line with the fact that the ingestion of soluble carbohydrate changes the reaction of the rabbit's intestine from alkaline to acid. Perhaps it is the acid reaction of the intestinal contents that inhibits the growth of putrefactive bacteria. Exercise, by causing more rapid absorption

of water from the intestine, may decrease the growth of bacteria, whereas in diarrhea the increased fluidity increases bacterial growth.

Besides the common bacteria of the intestine just mentioned, that are always present, and whose relative numbers depend on the soluble carbohydrates present, other bacteria that are normally absent appear as infections, as, for example, the typhoid and paratyphoid group. It seems possible, also, that other less virulent, unidentified bacteria may play a part in altering the normal conditions of nutrition.

COOKING. In *The Complete Cook*, 1805, which is the revised and corrected edition of *The Frugal Housewife*, the following sentence may be found in the preface: "The chief excellence of all cookery consists in a perfect acquaintance with the making of gravies and sauces." That is not the aspect of cooking to which reference will be made. The natural flavors of foods with the addition of salt, which is a necessary ingredient of the diet, should be sufficiently attractive to the hungry man. The necessity of cooking lies in two circumstances: (1) it is necessary to gelatinize the starch in starchy foods in order to make it utilizable and (2) it is desirable to kill certain pathogenic organisms or destroy bacterial toxins when present. Most starches gelatinize in water of 70° C. in a few moments, and prolonged cooking is only necessary in case the food is so dry that prolonged soaking is necessary to wet it (and the heat merely shortens the time necessary to soak it). Cooking softens food so that it is easier to chew, but that may not be wholly desirable. If it is desired to gelatinize collagen a high temperature or prolonged duration is necessary, but gelatin is too deficient a protein to be much sought after.

Many persons who would not eat a rare steak see no necessity in cooking canned goods. From the standpoint of danger from bacterial agencies, however, it is more necessary to sterilize preserved foods than fresh ones. Many cases of botulism are due to eating canned foods or tasting them to see whether they are spoiled, and it is stated that cooking destroys the toxin of *Bacillus botulinus*. Since cooking reduces the vitamin content of foods any unnecessary cooking is to be discouraged. Fresh foods if kept clean should be eaten raw or rare, whereas preserved foods, as a rule, should be cooked. Pork and fish should be sterilized because they are liable to contain parasites that escape detection. Mixtures of meat and vegetables should not be allowed to remain long uncooked, because numerous spore-bearing bacilli on the vegetables multiply rapidly in the meat juices.

Many persons object to visible fat in cooked food; in fact, some cooks remove fat from the surface of soup with blotting paper. Fried foods are said to upset delicate stomachs, and this has been attributed to the action of heat in setting free fatty acids. It has been shown, however, by the War Committee of the Royal Society

that free fatty acids in relatively large quantities may be eaten without disagreeable effects. Perhaps the irritant action of some fried foods may be due to the formation of acrolein. Since this occurs only in case the temperature is raised to 300° C., there is no necessity for it. The fat of all foods should be eaten as an economical measure.

FOOD PRESERVATION. The most ancient and widely used method of food preservation is by desiccation. The seeds of plants are usually desiccated before they are gathered for food. The desiccation of root vegetables was practised by various savage tribes and the drying of meat and fish was perhaps as common a practice. Hawk calls attention to the fact that dehydrated vegetables when soaked up again hold their water much less tenaciously than fresh vegetables do. This has been known as a characteristic difference between live and dead tissue, and the living state is associated with electrical polarization of the cell surfaces, which would partially explain the holding of water. In fact, it is the tenacity with which foods hold to water that adds largely to the cost of dried foods. In the drying of prunes, decomposition usually takes place unless the prunes are first dipped in an alkaline solution, so as to make them permeable to water. In the desiccation of tissue for biochemical analyses it has long been known that decomposition of phosphatides and oxidation of unsaturated fatty acids occurs if the moist or dried tissue is exposed to air, and similar decomposition must occur in dried foods.

Various forms of pickling and preserving in which the addition of salt or sugar occurs is similar to drying, in that the antiseptic action of salt and sugar is partially due to their dehydrating effect on bacteria. The use of other antiseptics is so limited as to be of minor importance.

The process of canning might be considered next to refrigeration in excellence as a method of preserving food, but unfortunately, complete sterilization and exclusion of air does not always occur. In the canning of milk, partial desiccation is also performed.

In the process of cold storage, vegetables and fruits remain alive, and it is claimed that fish may be kept alive in cold storage by the Pictet process. The growth of penicillium on beef in cold storage hastens ripening and the beef does not become toxic until the taste changes to musty or bitter. Beef is the best meat for cold storage on account of its large size and low water content and mechanical density, which inhibit the penetration of microorganisms. Cold storage is the only method of food preservation that maintains the total vitaminic content.

PROTEINS, FATS, CARBOHYDRATES, SALTS AND WATER. The protein factor in nutrition has been so exhaustively treated by Osborne and Mendel and others that it cannot be reviewed here. A general rule animal proteins are more complete in amino-acid

content than are those of vegetable origin. According to Goldberger, Wheeler and Sydenstriker, families in which pellagra occurred consumed 3 ounces of protein per man per day, but only 25 per cent. of it was animal protein. Since a nitrogen balance may be maintained in skinny individuals on less than 3 ounces of protein per day, we may assume that 3 ounces is sufficient, provided it is all animal protein; but that in case of mixed proteins, and in the absence of more definite knowledge, it is not wise to make a special effort to limit the protein intake. Under modern conditions there seems to be no defence for vegetarianism. Clark finds a high protein diet increases the rate of healing of wounds. It is also useful in case of profuse pus formation to replace the lost protein.

In addition to the fact that some fats contain vitamins, fats are necessary in the diet to decrease its bulk. In a diet of 3000 calories it would require 10 pounds of potatoes or other vegetables or fruits for the three meals, and if we include the saliva and other fluid swallowed and the gastric juice secreted the stomach would receive a load of about 8 pounds per meal (not all at once, however). Hardtack would be less bulky, but would increase salivation and thirst. The Interallied Scientific Food Commission fixed the minimum fat ration at 75 grams.

So far as investigations have progressed, muscular work depends on a supply of carbohydrate (compare Anderson and Lusk). In the absence of carbohydrate, fat is incompletely oxidized (for heat production) and yields products that may be toxic. Both man and the dog may live for considerable periods without carbohydrate in the food and probably depend for muscular energy on the carbohydrate radicle of phosphatides and glycoproteins and especially on the synthesis of glucose from glycerin and deaminized amino-acids; but there seems to be no advantage in such a diet. The flooding of the intestine with soluble carbohydrate retards putrefaction of proteins.

Salts are necessary, but since all factors causing their excretion have not been thoroughly investigated the minimum requirement is uncertain. Sodium chloride should be added to food, but it seems probable that the other salts are present in a mixed diet in sufficient quantity. Since milk and fresh vegetables that are rich in salts are also rich in vitamins that cause relative retention of salts, all that can be said is that milk and fresh vegetables are advantageous, and we are not justified in substituting an inorganic salt mixture for them. No harm can arise, however, in the addition of such a mixture to an apparently adequate diet.

The necessity of water in the diet needs no comment, and Hawk and his collaborators have shown that no ill-effects follow water-drinking at meals. The salt content of drinking water is usually insignificant, and the arguments for lithia water have been shown to be fallacious.

VITAMINES. Owing to the fact that differences of opinion exist among investigators as to the number of vitamins, the classification made by the British Committee on Accessory Food Factors will be followed. Hopkins studied "Accessory factors in food." Funk called these vitamins, and McCollum and Kennedy claim there are only two vitamins, which they call fat-soluble-A and water-soluble-B. Drummond refers to the antiscorbutic factor as water-soluble-C. McCollum and Kennedy's A-factor is also called fat-soluble or antirachitic vitamin, and their B-factor is called antineuritic vitamin, whereas Drummond's C-factor is usually called antiscorbutic vitamin.

The fat-soluble or antirachitic vitamin is very abundant in yellow fats of animal origin. It is deficient in pig fat because the pig eats few leaves, and in hydrogenated or hardened fats and free fatty acids because it is destroyed by the heat and chemical agents used in manufacture. It is deficient in vegetable fats except perhaps in peanut oil. It is synthesized in green leaves, and carnivorous animals depend for their supply on the bodies of grazing animals in which it has been extracted from the green leaves eaten and stored in the body fats. It is abundant in the germ of seeds, especially yellow seeds but deficient in degerminated cereals. It is present in potatoes, carrots and bananas, being most abundant in the yellow colored roots (carrots and sweet potatoes). According to McCollum the milk of cows is richer in fat-soluble-A when more is present in the cow's food. According to Osborne and Mendel, 1916, this vitamin is not destroyed in butter fat by storage for a year. According to Drummond, fat-soluble-A is not carotin.

The antineuritic vitamin seems to be most concentrated in the seeds of plants and eggs of animals. In cereals it is present in the germ but absent in the endosperm and bran (unless the bran contains the germ. It is abundant in yeast and in animal gland tissue, but muscle tissue and milk do not contain an oversupply. Both leaf and root vegetables and fruits contain it in small amounts. Cooking reduces the quantity of this vitamin. As first observed by Frazier and Stauton the content of food products from the same source in this vitamin runs parallel to the phosphorus content. According to Voegtlin and Myers, both antineuritic and fat-soluble vitamins of wheat and corn products run parallel to the phosphorus content.

The antiscorbutic vitamin seems to be present in all living tissue and fresh food, and is especially abundant in acid fruits, tomatoes, cabbage and turnips. It is more or less abundant in all fresh, raw vegetables. It is very sensitive to alkali, heat, desiccation and storage at ordinary temperatures, and hence is deficient in cereals and dried or canned meat and vegetables, except canned tomatoes. The acid in tomatoes and fruits seems to protect it during the heating and it is useful to class tomatoes with fruits, as

is done by British writers. It is present in milk in small amounts. Dutcher has shown that young guinea-pigs grow better and are healthier on milk from a cow on green feed than of a cow on dry feed. Scurvy developed very quickly on winter milk, but did not develop (in the same length of time) on summer milk. The milk was skimmed in both cases to prevent diarrhea. This indicates that the antiscorbutic vitamine in milk depends on that in the cows' feed, and may explain why some breast-fed babies have scurvy if the food of the mother is deficient in antiscorbutics.

VITAMINE REQUIREMENTS AND DEFICIENCY DISEASES. Since the composition of vitamins is unknown and their distribution among foodstuffs is known only in a general way, it is not yet possible to work out the vitamine requirements with even as much certainty as has been done in the case of food constituents of known composition. Experiments on animals and observations on man indicate that vitamine deficiency manifests itself more slowly the longer the average life (in different species) and the more mature the individual (in the same species). It is also necessary to know that the individual has been getting an adequate supply of vitamins before the beginning of the experiment in order to determine the duration of vitamine deficiency that it can stand. Even with this precaution, variations in results may be obtained owing to lack of knowledge of the degree of vitamine deficiency in the food. At present the vitamine content of foods can only be determined by the quantity of the food necessary to prevent or cure deficiency diseases. Hence the vitamine requirement may be estimated only in terms of the proportion of vitamine-containing foods required in the diet.

That the deficiency diseases are due to lack of vitamins can be determined only by the method of exclusion. Almost every imaginable cause has been attributed to the deficiency diseases, and some causes have been proposed that it is impossible for me to imagine. For instance, scurvy has been attributed to lack of ionization of the salts in the food due to staleness, and it is impossible for me to imagine a lack of ionization of these salts in food that has been eaten, and certainly food will not hurt you if you do not eat it. Scurvy has been attributed to an acid-forming diet, but McCleendon, Cole, Engstrand and Middlekauff have shown that this factor is not responsible for scurvy. The germ theory of these diseases will probably be popular for a long time, since bacteria are always present, waiting for an opportunity to hasten the death of a weakened individual. It is therefore useful for purposes of discussion to include among deficiency diseases those that have been cured in the presence of a vitamin-rich diet and have not been cured in the absence of such a diet. We will consider deficiency diseases of infants and adults.

Rickets is perhaps the most common deficiency disease, frequently occurring in breast-fed infants. To quote a book written before Funk's ideas of vitamins were generally known, Miller states that, without doubt, rickets is to be regarded as a dietetic disease, and considers deficiency of butter fat as the most constant and potent cause. In treatment, among other things, he recommends milk, cream, butter, egg yolk and cod-liver oil. These fats are especially rich in the antirachitic vitamin. Since the bones are softened in rickets the child may not be able to take proper exercise or go out into the fresh air, hence the view that rickets is due to lack of exercise or fresh air. The mother's milk might be sufficient in antirachitic vitamin, and yet the child may have rickets, due to the fact that it was weaned too soon. The Fijians, who included some of the finest specimens of physical development in the human race, nursed their infants for three years, and as the mother's milk became deficient in quantity, supplemented it with bananas. Rarely a mother in this country nurses her children for three years, but in savage Fiji it was a religious custom, and the taboo was placed on the mother in order to prevent the interference of the father. The prevalence of rickets among negroes may be due to the fact that the mother's diet of corn bread and fat pork is deficient in antirachitic vitamin. The British Committee base their statements concerning rickets on the experiments of Mellanby on pups. Hess and Unger failed to cure rickety babies on cream, but did so on cod-liver oil.

Xerophthalmia, keratomalacia or xerosis conjunctivæ infantum, an eye disease of infants that has been especially prevalent in the Scandinavian and other European countries during the war, is due to lack of antirachitic vitamin, the deficiency probably being greater than that required to produce rickets. It is accompanied by diarrhea. Sztark cites a case that developed after an exclusive diet of pea soup for fifteen months, and was cured in ten days on a diet of cows' milk.

Infantile beriberi occurs in infants nursing from mothers who have the disease, and whose milk is consequently deficient in antineuritic vitamin.

Infantile scurvy is due to deficiency of antiscorbutic vitamin. To quote again from "previtamin literature" Miller states that the opinion most commonly held is that scurvy is caused by a diet which through sterilization has been deprived of its "fresh element" and recommends orange and grape juice in its treatment. The fact that scurvy may occur in breast-fed infants, indicates variations in the antiscorbutic content of milk.

Marasmus is often considered a dietetic disease. Miller states that not seldom the child has thrived on the breast for a month or two, and has then been weaned in order that the mother may go out to work, and from that time has gradually wasted. Eddy and

Roper claim that the addition of a powder rich in vitamins to the cereal food of marasmic babies increased tissue growth. Vitamins are certainly necessary for growth, but so are other food constituents.

Since the question of growth has been referred to, perhaps it is well to remember that for normal growth there is necessary not only vitamins, but also the secretions of ductless glands. It is well-known that the size of the ductless glands is greatly affected in deficiency diseases in man and animals. According to McCarrison, deficiency of vitamins in the diet leads to abnormalities in the secretion of the ductless glands. We know that iodine in the food is necessary for the normal functioning of the thyroid, and it is possible to imagine unknown constituents of the diet that may be necessary for the ductless glands.

Pellagra may occur in breast-fed infants whose mothers have the disease, but it usually takes a long time to develop.

Deficiency diseases of adults may be different from those of infants, because growth is complete, although many of these diseases characteristic of adults occur also during adolescence or infancy.

War edema, also called famine edema or hunger edema, has been ascribed to lack of the antirachitic or fat-soluble vitamin, or other element in the diet. The fat content of the diet in war edema is not accurately known, but Guillermin and Guyot state that the total ration was sometimes as low as 800 calories, and it contained a very small proportion of fat, and that a decrease of 40 per cent. in body weight was common. Park has shown that it is readily cured by a return to the normal diet. War edema, or famine edema, as it is more often called, is not a new disease. Lusk refers to an account of it in France in 1817, just 100 years previous to the late outbreak in Germany and other European countries and Mexico. He also states that cases were cured in a week by the addition of 100 grams of fat to the ration. It is stated that edema occurs when there is a decrease in blood-plasma proteins, and hence that decrease in protein in the diet may cause edema. A diet of 800 calories fed prisoners is naturally deficient in protein. The scorbutic symptoms observed by Beyerman in famine edema suggest scurvy or a complication of scurvy. He states that the edema was cured by adding vegetables to the diet. Edema occurs in various deficiency diseases, and hence some confusion may arise in the classification, but the large number of cases of war edema that have occurred recently, indicate that it is a separate disease. Schittenhelm and Schlecht observed decrease in blood proteins in war edema.

Beriberi is a form of multiple peripheral neuritis caused by a deficiency of antineuritic vitamin, and is most prevalent in rice-eating countries. Wet beriberi is accompanied by edema, but in dry beriberi this is substituted by atrophy. As is often the case

in deficiency diseases, there may be gastro-intestinal disturbances. The principal cause is too exclusive a diet of polished rice, and according to Fraser and Stanton, the substitution of undermilled rice, containing at least 0.4 per cent. of phosphorus, prevents the disease. It may be caused by too free use of any degerminated cereal. The addition of canned goods to the diet may not prevent it. There is apparently not enough yeast in bread to prevent beriberi. Beans and peas are perhaps the most useful preventives. In the treatment of the disease, extract of rice-polishings and fresh yeast or autolyzed yeast have been used. Funk, Iyle, McCoskey, Caspe and Poklop observed a mild glycosuria in man on a diet of white bread and polished rice.

Scurvy was perhaps the first deficiency disease to be recognized as such. Captain Cook showed that it could be prevented by the use of fresh vegetables. Nansen and Johansen passed a winter on an exclusive meat and fat diet without scurvy. Stefansson claims to have cured cases of scurvy by a raw meat diet. Apparently all fresh foods have traces of antiscorbutic vitamine. The juice of sweet limes or lemons is especially rich in this vitamine, and this fact has led to the development of a large industry for bottling lime juice. This preparation was not tested until recently, and was then found to be deficient. By some mistake, sour limes have been substituted for the curative sweet limes, and the lime juice of commerce does not come up to expectations.

Pellagra was called alpine scurvy by Italians, and has been shown by Goldberger to be a deficiency disease. By definition the disease is characterized by a symmetrical dermatitis, especially of those parts exposed to the sun, but this is not its most serious characteristic. The worst features of beriberi, scurvy and pellagra are the effects on the nervous system. The hemorrhages in pellagra are in the nervous system, whereas in scurvy they are general (and may occur in the meninges). Sundwall has shown that the tissue changes in pellagra are not specific, but are similar to those in animals on inadequate diets. In beriberi, pellagra and scurvy gastro-intestinal disorders are present. In pellagra edema is extremely localized, in scurvy it is associated with hemorrhage and in wet beriberi it is more general. Pellagra is of very wide distribution and may be worldwide. Since a patient with pellagra may live ten years, it is probably not due to complete absence of any dietetic constituent but to a slight deficiency. Whether this is a vitamine or an amino-acid, or both, has not been determined.

Trench foot is attributed by Bruntz and Spillmann to lack of vitamins associated with life in the trenches, the predisposing cause being the diet, and the water-filled trenches causing the acute symptoms in the feet.

Sprue was classed as a deficiency disease by Cantlie, who found scurvy in some cases. Brown states: "In the open alluvial workings

of a tin mine in the East Indies all of the employes are exposed to the same atmospheric conditions. The Chinese coolie is stricken with beriberi, his European overseer with sprue. In no essential condition, even in that of diet, are the circumstances of their daily life materially different. The treatment of sprue is essentially dietary. A milk diet, a raw fruit diet, a milk and fruit diet or a raw or rare meat diet is used. In any case the diet contains vitamins."

VITAMINES AND APPETITE. In all animal experiments on a vitamin-deficient diet loss of appetite occurs. With human beings, psychological factors may enter in so as to make it difficult to perform clean-cut experiments on this subject, yet the final loss in tissue substance in all deficiency diseases suggests that the appetite has been affected. We know that pure proteins, fats and starches have no taste, but we do not know whether vitamins have flavor. We do know, however, that the taste of milk changes on boiling and the taste of many foods changes by canning or drying. Why is it that some persons have been known to defy the cholera germ for a raw oyster and the typhoid germ for a salad, and to give their lives for a momentary tickling of the palate? There must be some great advantage in fresh foods or else the desire for them would be eliminated by natural selection. To the clothes-moth the age of food seems to make little difference, but when a man sits down to a meal of storage eggs, canned milk, jerked beef and hardtack it requires considerable hunger to whet the appetite. This craving for fresh food has probably saved more lives than are killed by germs. The human race has existed for some time prior to the advent of food chemistry, and most people live nowadays without the aid of that science. Unquestionably the appetite has played some part in the preservation of the race. It seems probable that the person who is presented with an adequate choice of natural foods from infancy will choose an adequate diet, and that the cause of the deficiency diseases is that an adequate choice of foods is not always supplied to the table. In the case of animals this question has been tested. Evvard allowed pigs free choice among a variety of foods, and in this way produced the largest pig for its age that was ever raised at the Iowa Experiment Station. A more rigorous experiment was made by Osborne and Mendel, since they did not use natural foods but purified components made into a biscuit. A rat presented with a more and a less adequate biscuit might eat for a few days from the less adequate, but finally showed preference to the more adequate diet. These experiments did not refer to vitamins exclusively, but they show that an inadequate diet results in some change in the appetite.

FOOD SUBSTITUTION. According to Steenbock, fat-soluble-A is more abundant in yellow foods than in corresponding white ones. Yellow corn contained more than white corn, yellow oleo oil more than white fat separated from the same adipose tissue, yellow

sweet potatoes more than white potatoes. The artificial coloring of butter may therefore deceive us as to its vitamine content. Without doubt the operation of the Pure Food and Drugs Act and the work of the laboratories operating under this law have been of inestimable advantage to the public. Food chemistry has not reached a sufficient stage of development to be relied on exclusively in questions of food substitution. Feeding tests are necessary, and the preference of the public for natural products, on which feeding tests have been made by the human race, is well grounded. The work of food fakirs has been insidious. Take the question of oleomargarin. The early products coming under this label in this country contained a large percentage of oleo oil, which is rich in the fat-soluble vitamine. Little by little the proportion of such oleomargarins has decreased and perhaps the majority of oleomargarins today are made from cottonseed and coconut oils and are deficient in fat-soluble vitamine. Galicians eat lard on their bread, but it is said that the black bread they use contains some fat-soluble vitamine from the rye germ. Negroes have a particular fondness for pork fat and white cornmeal bread, and this may be the chief cause of the prevalence of rickets in negro babies, since the diet of the mother does not contain enough fat-soluble vitamine to be transmitted to the milk. In a milk-canning factory in this country, skimmed milk and vegetable oils were run through a homogenizer and canned as milk compound. The cook may see the label on the artificial milk or butter, but the defenceless boarder does not even have the satisfaction of reading his sentence. Another deception is the soaking of dried green peas in water and then canning them. The Pure Food and Drugs Act does not allow the picture of a pea-vine to be placed on these cans, but the average consumer is not familiar with such distinctions in labels.

In natural foods a sweet taste is associated with fruits that are rich in antiscorbutic vitamines. If we may suppose that the taste for sweets is inherited, our savage ancestors may have eaten raw fruits, just as the monkeys in the jungle do nowadays. Most of the sweet food and drinks of modern man are made from sugars and molasses and honey that are free from vitamines. Coffee and its substitutes and tea, malted or distilled liquors, wines and carbonated drinks with synthetic flavors are deficient in vitamines.

I ordered a meal in a "pure food restaurant" and received various fake dishes, including an imitation beefsteak made of degerminated cereals. The fact that we use milk with cereals is probably what saves us from disaster. One is reminded of the old story of the soup-stone: A man knocked at the kitchen door and said he was introducing soup-stones. The stone was to be boiled in water, and he demonstrated it to the housewife, suggesting various ingredients that might be added to it. These were promptly produced by the enthusiastic housewife and the man drank the soup,

leaving her the stone. Cereals form the basis of our diet, but scurvy develops when they are used as substitutes for potatoes or other vegetables, as occurred in Glasgow, Newcastle and other cities during a potato shortage during the war. In one institution in the United States there were 200 cases of scurvy on April 1, 1916, following two months' reduction of the potato and other vegetable ration to one-half.

THE MILK QUESTION. The rise in the cost of living, more than the rise in the cost of milk in particular, has led to a reduction in the consumption of milk by families with small incomes. Harris records data from 2084 families, representing in nationality and income a typical cross-section of New York City in the summer of 1918. In 14 per cent. of these families milk was entirely eliminated from the children's dietary. McCollum has repeatedly emphasized the advantage of milk in the diet. Mendenhall states that every child from eighteen months to twelve years of age is better for having one and a half pints of milk in its daily diet, and that fluctuations in the demand for milk or diminished use of milk throughout the country will inevitably result in a lessened production, and that the loss of our herds at this critical period would be a calamity. Hart and Steenbock call attention to the use of milk as a supplement to cereal foods. Milk makes up the deficiency of cereals in vitamins, salts and certain amino-acids of the proteins. The United States Food Administration calls attention to the fact that milk compares favorably with other animal foods in price per gram of protein and in price per calorie, and that there is only enough milk consumed in this country to give each person a little more than half a pint per day. Twenty and more years ago a professor of mathematics used to tell a story of being hard up in his college days. He calculated that he would have ten cents a day to spend for food, and that the highest nutritive value could be gotten from ten cents' worth of milk. Practical experience, however, suggested a change to five cents' worth of milk for nourishment and five cents' worth of mince pie to "stay with" him.

The chief value of milk lies in the fact that it is a complete food and does not require any balancing of components or any precautions to include the minimum requirement of any constituent. I have never found a species of cooks who would calculate or weigh or balance any food constituents except under immediate compulsion. With a milk diet for the infant and a modicum of milk in the diet at all other ages the expense of calculation of dietary constituents is eliminated, and milk even at a high price may be worth buying in order to avert the danger of malnutrition and doctors' bills or loss of efficiency. It is an open question, however, whether cows' milk has been beneficial to infants in general. During the famine resulting from the siege of Paris the infant mortality fell 40 per cent., due to the fact that mothers nursed their own infants. A similar

decrease occurred during the great Lancaster cotton famine, due to the fact that the mothers could not work in the factories and did not have the money to buy cows' milk for the infants. During the recent occupation of Lille by the Germans, when the adult population lost about 40 per cent. in weight, there was a reduction in infant mortality, due to the fact that the mothers nursed their own infants. In the absence of mothers' milk, however, cows' milk is the best food for infants, but it is better to feed the cows' milk to the mother if she can nurse her child.

ARMY RATIONING. It seems probable that the chief point of attack of faulty nutrition on the military strength of a nation is on the infant males. Crooked bones, bad teeth and other deficiencies may result from faulty feeding of prospective soldiers. If the soldier going into action has a well-nourished body to begin with a short campaign on very defective rations may not lead to serious consequences. The protein, fat, mineral salts and vitamins stored in the body may be drawn on to make up the deficiency. It is often stated that the body cannot store protein, and it is true that protein is not stored in the same way that fat is; but the protein of the muscles may be drawn on for a considerable period, as has been the case in millions of persons during this war.

The ration allowed the army by Congress has been subject to many variations. The soldier eats what he can get, but must necessarily be influenced by the ration allowance. During the Revolutionary War conditions were very variable. In 1780 the American Army was increased by the addition of the French Division (5000 men), who landed from transports with over 600 cases of scurvy among the soldiers and 1000 cases among the sailors after a voyage of two months and nine days.

In 1775 fresh milk was included in the army ration, but since it could not always be supplied a revision of the ration was soon necessary. In 1798 Congress fixed the ration at 20 ounces of beef, 18 ounces of bread and an allowance of salt, soap and candles. Food profiteers made a liberal interpretation of the words "bread and beef," so that the Surgeon-General thought it necessary to report unfavorably on the results. The two staple articles of the ration have remained practically unaltered in quantity until the present day, but later Congresses allowed liquor and specified substitutes for beef. In 1818 the President was authorized to make changes in the ration other than increase in cost, and in 1834 he substituted coffee and sugar for the liquor component. Temporary increases for the period of the Civil War were made, but except when raids were made on food stores the nutrition of the troops was not ideal. Owing to the large proportion of preserved food, including flour, salt meat, desiccated vegetables, canned milk and coffee extract, 30,741 cases of scurvy were recorded among white troops. In 1890 a pound of fresh vegetables was added to the ration

and in 1908 the present garrison ration was authorized, which is of sufficient cost and allows sufficient substitution to furnish an adequate diet. The savings privilege in rationing in garrison, authorized in 1910, was abused to such an extent that it was discontinued April 1, 1919, and all substitutes are purchased through the quartermaster and the savings revert to the Government.

About the only data we have of the nutritive balance of our soldiers are their weight records. According to Munson the average peace-time recruit gains about 2.8 pounds in the first three and a half months of military service. Similar figures for the National Army, compiled by Hildebrandt, show a gain of 6.4 pounds in the first four months of military service. The total gain during the war has been reported as twelve pounds per man. Such figures are encouraging, considering the fact that some of the recruits were undernourished at the time of enlistment. If the added weight is not necessary for muscular strength it is useful in raising the resistance to disease and famine. The army has experimented with an emergency ration, consisting of a dried mass of chocolate, eggs, milk and sugar that has a high protein and calorific value, but no one has been able to eat it for more than three successive days. When water only is available a reduction of a pound a day in body weight occurs in warm weather and more as the weather turns colder, and a few pounds excess body weight form the best emergency ration, since accidental loss is eliminated. Owing to the fact, however, that carbohydrate is stored to a very limited extent in the body, the use of hardtaek, if available, is advantageous.

I have had opportunity to compute the protein, fat, carbohydrate and total calories per man per day in a large number of army messes and have studied the data compiled by the Food Division, and in the majority of the few cases of deficiency noted, have found that the mess sergeant was inaccurate in his accounts or was trying to produce an impression on the inspectors. In some cases the soldiers and their mess officers complained of the food. The chief ground of complaint was that there was not a sufficiency of fresh fruit and vegetables. I computed the mineral constituents, and especially the acid-base balance, of these messes, and found them usually acid. Certain foods, however, which yield a basic ash (dried beans, for instance) were served too frequently to please the soldiers. It was not the character of the ash of the food which influenced their comment, but its freshness. Certain national guard companies had company funds sent them from their home towns. I found some of these companies at Camp Cody, N. M., spending thirty cents per man per day for fresh milk and a more variable sum for fresh California fruit. A certain officer having about 2200 men in his command found inefficiency in one or more of his mess sergeants and decided to run the messes himself. He made up bills of fare for twenty-one meals and ordered all mess

sergeants in his command to use them. The foods listed were those carried by the quartermaster and there was a conspicuous absence of the fresh fruits and vegetables of the local markets. I found the order to use the menu evaded more frequently the farther the mess was from headquarters, and at the end of ten days the scheme was abandoned. If the desires of the soldiers may be expressed in chemical terms, they desired vitamins, and especially antiscorbutic vitamins.

Whereas the ration allowance for soldiers on duty has been based on the price of food, and the same was originally allowed for sick soldiers, during a certain period each base hospital was allowed a fixed sum of money for each sick soldier on its rolls. On June 1, 1918, the ration allowance for a sick soldier was fixed at fifty cents. In some of the larger hospitals savings were made, but the smaller hospitals reported that the allowance was not sufficient. I have no records for the same hospital covering a long period, but by combining data from three hospitals some comparisons may be made. These data are from Camp Pike, Ark., June, 1918, Camp Cody, N. M., August, 1918, and Camp Fremont, Cal., November, 1918. During this period there was a general rise in the cost of food, and to meet this, reductions in the higher priced articles of food were made. In June 13 ounces of fresh meat per ration were served, in August 7 ounces and in November only 3.2 ounces. In June 2.5 eggs per ration were served, in August 1.2 and in November 0.4. At Camp Fremont from August 1 to September 1 the rise in price of fresh eggs was from 52 to 89 cents per dozen, of fresh milk from 23 to 40 cents a gallon and of oranges from 6 to 13 dollars a crate. At the end of this period the fixed allowance was superseded by a sliding scale system based on the local cost of the garrison ration plus a certain percentage that was greater the smaller the hospital.

The above remarks apply to the army in this country, but the United States troops in other countries have not always fared so well. Beriberi among the Philippine scouts gave occasion for an order that the meat ration was to be eaten and that the rice was to be undermilled (Chamberlain). Riddell, Smith and Gutierrez reported 60 cases of beriberi in the United States Army in Porto Rico November, 1918. Potatoes, beans and canned meats and vegetables were supplied the troops, and these data led to the supposition that the reduction in vitamins by canning may have been a factor.

The fly problem is serious in the army. Ball has shown that the house-fly may be carried 100 miles by the wind. I have seen squads of soldiers swatting flies in mess halls when the civil authorities allowed a mountain of horse manure to remain two miles outside of camp.

DISCUSSION. Observations, some of which are reported in this paper, have led me to believe that the nutrition of some individuals,

especially infants, is not ideal, and that the high cost of living is leading to worse nutrition. A large part of the population has unconsciously depended on the presence of milk in an otherwise inadequate diet, and the decrease in milk consumption that is now taking place is to be viewed with alarm. The supply of fresh green vegetables is not sufficient to be a substitute for milk. Grass is not adapted to human alimentation except in the form of sprouted grass seeds. In the sprouting of seeds vitamins are synthesized in the young leaves and a quick crop of vitamins may be obtained without the necessity of planting the seeds in the ground. McCleendon, Cole, Engstrand and Middlekauff have most recently studied the question of sprouting cereal grains. Wheat or rye, sprouted until the shoot extends an inch beyond the grain and heated in water to 70° to gelatinize the starch, forms a cheap and convenient and palatable source of vitamins. The seeds may be freed from bacteria before sprouting (Braun and Duggar and Davis). Since beef fat is about as valuable a source of vitamins as butter is, beef drippings and fat should be eaten rather than thrown in the garbage can, and the same applies to some other animal fats. Prolonged cooking of fresh foods should be discouraged, but all canned goods should be heated to boiling before serving, in order to destroy toxins of *Bacillus botulinus* that might be present, unless a competent inspection of the goods has been made.

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THE CURE OF HOOKWORM INFECTION.¹

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DURING the recent war there were admitted to the author's gastro-intestinal service at the United States Army General Hospital No. 14, Fort Oglethorpe, Georgia, 393 cases of ankylostomiasis, over one-fourth of which had received previous and obviously unsuccessful hookworm treatment. This large proportion of failures is due, in our opinion, (1) to the real difficulty of achieving a complete cure quickly by the methods of treatment heretofore in vogue, and (2) to the lack of sufficient observation after treatment, owing in turn to the absence of satisfactory scientific data on which the precise criteria of cure could be based. It has been our endeavor to remedy both these defects, the former by the development of the intra-intestinal tube treatment already described² and the latter by means of the most intensive studies of the results of therapy that we could possibly make under army conditions.³

As soon as a hookworm suspect was admitted to our service, and before any treatment was given, stools were sent daily to the laboratory until the diagnosis was confirmed beyond question. After treatment, specimens were similarly examined, every other day, as a rule, until an interval of twenty-eight days had elapsed, unless they were reported positive before that. For the purpose of compiling the statistics presented in this paper, all incomplete observations have been entirely discarded. Our conclusions, accordingly, are based on 231 cases, all of which were observed twenty-nine days or over (up to two hundred and twenty-eight

¹ Read before the Duval County Medical Society, Jacksonville, Fla., Oct. 28, 1919.

² Kantor, J. L.: The Intra-intestinal Tube Treatment of Hookworm Infection, *Jour. Am. Med. Assn.*, 1919, *vol. lxxiii*, 1181.

³ At the time this work was carried on, Lieut.-Col. Calvin D. Cowles, Jr., of the regular army, was in command of the hospital. Dr. Lewis C. Eeker, of Washington, D. C., was in charge of the medical service. Drs. Burrill, Dunning, Paul, Hill, Hughes, Swan, Hagler, Rudbeck and Mahoney were at various times associated with the gastro-intestinal section. Dr. Le Roy Smith was in charge of the laboratory. The actual stool examinations, a task of great magnitude, were very capably performed by Mr. E. A. Piper.

days in one instance), and no case is reported as a cure that did not show an average of ten to fifteen consecutive negative stools during a period of four weeks after treatment. Some of the cured cases we were able to follow for a much longer time, one soldier having his twenty-fourth negative stool one hundred and thirty-six days after treatment.

The first problem that engaged our attention in a preliminary way was the absolute diagnosis of the existence or absence of infection in a given case. Thanks to Kofoid and Barber's loop-flotation-brine method of examining stools for ova,⁴ an extremely delicate laboratory procedure was already at our disposal. We accordingly endeavored to determine how many negative stool examinations should be demanded before a given Southern soldier could be pronounced hookworm-free. Obviously a single examination could not reasonably be expected to reveal every infection either because of errors unavoidable in a large series, because of very slight infections or because the worms were not constantly ovulating. The question was really one of importance not only because we had to be sure of our control methods, but because the reinfection of any case, treated or untreated, had to be taken into consideration. With these objects in mind it was arranged that all Southern soldiers admitted to the *medical* service of the hospital for the period of one month were to have their stools examined five times (on approximately five successive days) or until positive, whereas all patients admitted to the *surgical* service during the same period were to have but a single stool examination. As a result, of the 408 medical cases examined, 63 were found positive after the first stool, 17 more after the second, 12 more after the third and 3 more each after the fourth and fifth—a total of 98 positive cases, or 24 per cent. of the number examined. On the other hand but 32 of the 231 surgical cases were found positive with the single stool method, a percentage slightly under 14. In other words the five-stool method gave an increased incidence of over 9 per cent., and an increased efficiency (as between the two methods) of almost 40 per cent. To crystallize the importance of this, we found that one-quarter of the returning troops were still hookworm-infected by the five-stool method, whereas but one-seventh of the men would have been pronounced positive by a single stool examination.

In this connection it should be stated that the procedure recommended above is designed to reveal infections only in untreated cases or in those whose last treatment took place at least six weeks or two months before the examination. It is of course well known that vermifuges have the property of depressing the egg-laying function of parasites, but the exact duration of this "negative phase" in the case of the female hookworm seems to be a matter of uncertainty.

⁴ Kofoid, C. A., and Barber, M. A.: Rapid Method for the Detection of Ova of Intestinal Parasites in Human Stools, *Jour. Am. Med. Assn.*, 1918, lxxi, 1557.

In order to throw more light on this interesting question an analysis is presented of 100 cases which were reported positive after having received treatment on this service. (See Table I.) The drug used was oil of chenopodium in doses averaging 3. c.c. by tube and 2 c.c.

TABLE I.—SHOWING DAYS ON WHICH STOOLS FIRST BECAME POSITIVE AFTER 100 UNSUCCESSFUL HOOKWORM TREATMENTS.⁵

Days after treatment.	No. of cases positive.	Weekly total percentage.
4	18	} 1st week, 61
5	19	
6	13	
7	11	
8	3	} 2d week, 51
9	3	
10	4	
11	1	
12	4	
13	2	
14	2	} 3d week, 90
15	2	
16	2	
17	1	
18	1	
19	1	
20	2	
21	1	} 4th week, 98
22	2	
23	2	
24	0	
25	2	
26	1	
27	1	
28	0	
29	0	} 5th week, 99
30	1	
31	0	
32	0	
33	0	
34	0	
35	0	
36	0	} 6th week, 100
37	0	
38	0	
39	0	
40	1	

by mouth in capsules. Stools were examined every other day, and in many cases daily, until they came back positive or until an interval of at least four weeks had elapsed after the day of treatment. Since the roentgen ray and other means of studying bowel-emptying have shown that it may take up to seventy-two hours

⁵ Positive results within the first three days are disregarded. See text.

for the complete evacuation of a given meal, an arbitrary three-day limit was established, on the assumption that this would be sufficient for the discharge of all ova produced by worms that had been destroyed by the vermifuge. Accordingly, in the case of stools reported positive within this limit judgment as to cure or failure to cure was suspended until this interval was passed. Subsequently, if the positive results persisted, the case was pronounced uncured; or, if the stools remained negative *for at least four weeks*, the case was called cured. In every instance the period of four weeks was reckoned from the last positive stool, the total observation interval being thus lengthened to thirty-one days when the stool came back positive on the third day after treatment. It will be seen from a study of the accompanying table that observation for four weeks is by no means too long if one wishes to know whether a cure has actually resulted from a given treatment. As it is we have records of 2 cases which became positive only in the fifth and sixth weeks respectively, and by no means all our cases were observed for so long a period. In brief, 98 per cent. of our positive cases (or failures to cure) became such within four weeks, 90 per cent., within three weeks, 80 per cent., within two weeks and only 61 per cent. within the first week. It follows that an individual reported as negative within the first week after treatment may have more than one chance in three of coming back positive at some subsequent examination. That many cases were erroneously considered cured after a routine hookworm treatment as carried out in the various army organizations goes almost without saying. Moreover, when the question of reinfection arises one must be particularly careful that the original disease was actually cured in the first place.

In this connection we should like to point out still another possible source of error in diagnosticating the cure of hookworm infection. In their extensive study of this disease in the Orient, Darling, Barber and Hacker⁶ presented a method for grading the value of any particular form of hookworm treatment by comparing the number of worms removed by a first treatment with the total number of worms removed by subsequent treatments. This method was further developed into an "efficiency index" by Knowlton working in Kofoid's service.⁷ Admirable as this procedure is for a comparative study of treatment methods it should by no means be translated into a criterion of cure for the disease, the weak point in the efficiency index method being that further examination of stools presumably ceases as soon as any particular treatment fails to reveal the presence of worms in the excreta. As already explained in the author's previous communication all forms of treatment by mouth have the common objection that the vermifuge is not delivered directly at the site of infection. Hence the chance of

⁶ The Treatment of Hookworm Infection, Jour. Am. Med. Assn., 1918, lxx, 499.
⁷ Knowlton, R. H.: Hookworm Infection among Troops, Ibid., 1919, lxxii, 701.

missing the worms partially or even entirely is by no means merely academic. The following case is cited as an example:

CASE B 208.—Had three treatments, presumably by thymol, before entering the army.

Fourth treatment February 26, 1919, 2 c.c. oil of chenopodium in freshly filled hard, gelatin capsules. *Eighty worms recovered* from resulting stools. Subsequent stools positive for ova for eight days.

Fifth treatment, March 7, same as fourth, *eighteen worms recovered*. Subsequent stools positive on fifth and seventh days.

Sixth treatment, March 18, same as previous, *no worms recovered*. Stools, however, positive on second, third and sixth days.

Seventh treatment, March 27, same as previous *no worms recovered*. Stools positive on second, fourth and sixth days.

Eighth treatment, April 5, same as previous, *twenty worms recovered*. Stools negative for eight days more, at which point observation discontinued. Final result undetermined.

We were again and again impressed with this failure to cure after any of the usual forms of mouth treatment. Indeed, the same conclusion is reached from a study of any of the more careful work that has been reported in the literature. Thus in the severer types of infection encountered by the original Porto Rico Commission⁸ the majority of cases were not cured before four doses of anthelmintic had been administered and there are examples of twenty-two, twenty-three and twenty-five treatments being given without curing the infection. More recently the International Health Board, after a four years' intensive campaign in the West Indies,⁹ is able to report only 50 per cent. of cures after two treatments. Our own experience with the mouth treatment of the relatively mild infections found in the army was not very encouraging. Of the 87 cases treated by the mouth method (2 c.c. oil of chenopodium in freshly filled hard capsules) we could prove a cure in only one-half, this notwithstanding the fact that each man was observed and treated for a period of four weeks or more. If still positive at the end of this observation the patient was either discharged uncured or given tube treatment. As a matter of fact, 5 cases were still positive after six treatments, 3 after seven and 2 were left doubtful (owing to insufficient observation) after eight.

On the other hand our experience with the intra-intestinal tube method convinced us of its superiority over the usual forms of mouth treatment as a means for the rapid and complete eradication of hookworm disease. Of 137 cases treated by the tube we were able to prove a cure, despite the difficulties in observation, in over 87 per cent. Perhaps still more noteworthy is the fact that fully

⁸ Ashford, B. K., and Igaravidez, P. G.: Uncinariasis in Porto Rico, Senate Document 808, Washington Government Printing Office, 1911, p. 162.

⁹ Howard, H. H.: The Control of Hookworm Disease by the Intensive Method, Publication No. 8, Rockefeller Foundation, New York, 1919, p. 75.

80 per cent. were cured by the first treatment as compared with 34 per cent. by the mouth method. Furthermore, although the mouth method failed in our hands after even a sixth and seventh repetition only one tube case had to go on to a third treatment, the rest being cured in one or two sessions.

TABLE II.—SHOWING COMPARATIVE RESULTS OF MOUTH AND TUBE TREATMENTS.

Treatment.	No. of cases.		Percentage cured separately by each treatment.		Percentage uncured of all cases.	
	Mouth.	Tube.	Mouth.	Tube.	Mouth.	Tube.
1st treatment	35 ¹⁰	137	43	80	86	19 0
2d treatment	70	10	18	90	65	0 7
3d treatment	37	1	32	100	29	0
4th treatment	14		21		17	
5th treatment	9		11		9	
6th treatment	5		0		6	
7th treatment	3		0		2	
8th treatment	2		?		?	

It remains to point out still another advantage of the tube technic. It will be observed, by referring again to Table II, that 34 per cent. were cured by taking the first mouth treatment, 18 per cent. by the second, 32 per cent. by the third, 21 per cent. by the fourth, 11 per cent. by the fifth and none at all by the sixth, seventh and eighth. In other words the chances of being cured became progressively less hopeful as treatment was continued. This result is undoubtedly due to errors residing in the rationale of the mouth method, the reason for the fifth failure being just as great as for the first. Such a persistent disappointment might, for example, be due to the patient having achylia gastrica, in which case the associated hypermotility might carry the capsule far into the ileum before its dissolving. On the other hand the soundness of the principle underlying the tube treatment is further vindicated by what might be called its cumulative efficiency, 80 per cent. of the first treatments being successful, 90 per cent. of the second and fully 100 per cent. of the third.

Encouraged by the above experience the author feels justified in recommending the tube method as worthy of trial by the profession. Two treatments, given a week apart, should be sufficient to cure most cases. At first the method should undoubtedly be used only in hospitals, whether civil or military, or in the homes of patients.

¹⁰ Most of the previously *untreated* cases were given tube treatments, hence the relatively small number of first mouth treatments. On the other hand, almost all the previously *treated* cases were given mouth treatments with the exception of a few not included in this table.

After its safety and usefulness are further demonstrated by added experience, and perhaps after appropriate modifications and improvements in the technic, it may not be too much to hope that the tube treatment will ultimately become the method of choice in the eradication of hookworm infection.

SUMMARY. 1. An individual from a hookworm district should not be pronounced hookworm-free until a series of at least five negative stools has been obtained, and then only if the last treatment took place six weeks or more previously.

2. The "latent period" after treatment, *i. e.*, the period in which the egg-laying function of the hookworm is depressed by the vermifuge so that the persistence of worms cannot be revealed by stool examination, may extend up to six weeks. However the great majority (98 per cent.) of cases become positive again within four weeks after treatment.

3. The usual form of treating ankylostomiasis with drugs given by mouth has been shown to be unsatisfactory, even relatively mild infections resisting as many as seven or eight treatments.

4. Much more efficient results can be obtained by the method of intra-intestinal tube treatment, owing to the fact that the full, concentrated dose of vermifuge is delivered precisely at the point of infection. Instead of 34 per cent. of cures, as in the case of a first mouth treatment, fully 80 per cent. are cured by a first tube treatment. Only one repetition is necessary for the relief of the great majority of infections.

THE TREATMENT OF CATARRHAL JAUNDICE BY A RATIONAL, DIRECT AND EFFECTIVE METHOD.¹

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I DESIRE to present in this paper a rational, direct and effective method of treatment of catarrhal jaundice. I say a direct method to draw attention to the contrast between it and the usual symptomatic or expectant plan so commonly employed in treating these cases.

I will limit my subject to the treatment of catarrhal jaundice by this new method, with a passing allusion to the treatment of other more important conditions of the biliary tract.

The diagnosis of catarrhal jaundice, as a rule, does not offer

¹ Read before the Philadelphia Clinical Association October 27, 1919. This is the second of the series of articles on the diagnosis and treatment of diseases of the biliary tract.

many difficulties. This type of jaundice usually develops in a young person and more often in young men than in women. There is frequently a history of several days or weeks of a preceding gastro-intestinal disturbance, which with careful questioning can be traced to some definite cause. The patients are often conscious of the gastric discomfort, evidenced by epigastric distress and soreness after eating and associated symptoms of bad taste, furred tongue, increasing constipation, sour eructations, belching and flatulency. The jaundice appears gradually, usually noticed first in the whites of the eyes, often first called to the patient's attention by other people. Later there is a gradual deepening of the jaundice elsewhere. Less frequently the jaundice appears rapidly, almost overnight. The degree of jaundice varies in proportion to the catarrhal swelling of the common duct and the consequent degree of obstruction to the exit of the bile into the intestines. Even when the jaundice is extreme the symptomatic discomfort is relatively slight; increasing lethargy, mental hebetude, drowsiness, distaste for food and occasionally soreness over the liver. In the deeper states of jaundice itching of the skin may be troublesome and occasionally patients may complain of "seeing yellow." As a rule this is all. When in addition there is complaint of feverishness and chilliness and more definite pain there is probably infection plus catarrh. There is generally noticed jaundice, furred tongue, sore epigastrium, sometimes an enlarged liver, perhaps sore to heavy percussion. It is seldom that the gall-bladder is palpable or the spleen enlarged. The pulse is generally slow and the temperature is normal or subnormal. Objectively, too, we notice the bile-stained and scanty urine and the stools seemingly acholic. I say seemingly because on chemical and microscopic examination of the stool we may find that bile is coming through, although in lessened amount, and the pale, pasty appearance of the stools is due to the failure of fat digestion. Fermentation of the stool may be conspicuous and the odor is sour and offensive. Constipation is the rule, but there may be diarrhea due to the gastro-enteritis. The blood picture is normal, as a rule, except when the catarrhal jaundice is complicated by an already existent anemia or infection. The only constant abnormal phenomenon is the prolongation of the coagulation time. Cabot² calls attention to the frequency of the loss of weight that occurs during the course of many cases. This has not been conspicuous in the cases here reported. This is the picture of catarrhal jaundice. The diagnosis is usually confirmed by the benign course which rarely exceeds six to eight weeks even in untreated cases and the majority terminate in recovery. I do not intend to enter into a discussion of the differential diagnosis between "simple" catarrhal jaundice and the jaundice designated toxic, infectious,

² Differential Diagnosis, Philadelphia.

epidemic or metabolic, nor to discuss the validity of the so-called entity of Weil's disease nor to reopen the controversy between hepatogenous and hematogenous jaundice. It is interesting, however, to see the increasing tendency to consider jaundice, of whatever type, of hepatogenous origin. I do not desire to discuss the various avenues of infection of the biliary apparatus and their relative frequency. Suffice it to say that the gall-bladder and ducts may derive their infection through the portal veins, through the systemic blood, through the lymphatics, through the serosa from direct contact with infected neighborhood peritoneum, and finally by direct ascending infection of the common bile duct from the duodenal zone. I do desire, however, to emphasize the frequency of this last avenue of infection in catarrhal jaundice, based upon the study of this and other groups of cases.

For the proper understanding of the various conditions and infections of the biliary tract, reference is directed to the discussion of the subject by A. O. J. Kelly³ in his Mütter Lecture, delivered in 1905. An able article on epidemic jaundice has been contributed by Barker and Sladen.⁴ Their attached bibliography will serve to amplify our knowledge of this interesting condition. It is instructive to delve into the history of jaundice.⁵ The literature is simply voluminous, but we refer particularly to the monograph on jaundice by Harley,⁶ published fifty-seven years ago, the clinical lectures by Sir Henry Marsh,⁷ and to the exhaustive monograph of Legg, entitled *The Bile, Jaundice and Biliary Diseases*.⁸

My special concern is to bring forward a method of rational, direct and effective treatment of catarrhal jaundice. To treat disease intelligently and effectively we must have a rational conception of the life history and etiological and pathological factors of each given disease modified by an appreciation of the histology and anatomy of the tissues diseased. Our present conception of the pathology of catarrhal jaundice is that it develops from the extension of a gastroduodenal catarrh, passing upward into the terminal portion of the *pars intestinalis*, causing edematous swelling and congestion, and an increased production of mucus in the common bile duct, with often a plug of inspissated mucus corking up the ampulla of Vater. Owing to the exceeding rarity of deaths from catarrhal jaundice our opportunities to verify this conception at the postmortem table have been limited. Osler,⁹ however, observed a case which at autopsy showed the common bile duct obstructed with inspissated mucus at its terminal portion and slightly distended above. The hepatic duct

³ AM. JOUR. MED. SC., September and November, 1906.

⁴ Johns Hopkins Hosp. Bull., October, 1909, xx, 223.

⁵ Toxic Jaundice, Proc. Royal Soc. Med., October 1, 1916-1917.

⁶ Jaundice, the Pathology and Treatment, Walton and Maberly, London, 1863.

⁷ Clinical Lectures, London, 1867, vol. i.

⁸ Legg, J. Wickham: The Bile, etc., New York, 1880.

⁹ Practice of Medicine.

was also distended. More recently Eppinger¹⁰ described such an autopsy in which it was found that the occlusion of the common bile duct was due to a hyperplasia of the lymphoid tissue of the ductal mucosa, especially in that fraction of an inch which runs diagonally within the wall of the duodenum. He also found dilatation of the biliary ducts above this point. Eppinger and others believe that this lymphoid tissue acts as a defensive mechanism against infection, as does the lymphoid tissue in the tonsils, the bronchial lymph glands, the appendix, etc. The swelling, congestion and edema and mucous catarrh may progress higher in the common duct and into the cystic and hepatic ducts. This doubtless occurs in the cases of catarrhal jaundice of more prolonged duration, for it is easily conceivable that duration of the jaundice may run parallel to the extent as well as to the degree of duct catarrh. And what is the etiological factor primarily responsible for this catarrh? A catarrhal gastritis and a catarrhal duodenitis! There are no doubt mild cases of jaundice produced by pressure effects on the ampulla of Vater from edematous swelling of the duodenal mucosa alone without an extension of the catarrh into the duct itself. But what precedes the gastroduodenal catarrh? Surely dietetic indiscretions, exposure to cold and internal chilling and infection. I think we will find this true more and more frequently as we study our patients more closely.

Sixteen cases of catarrhal jaundice were observed and treated by me in Naval Base Hospital No. 5 in Brest, France, and were derived from officers and enlisted men chiefly engaged in destroyer duty. The destroyer service is always difficult enough in itself, but in patrol duty on the Brittany coast and in the Bay of Biscay in winter the weather is always cold and damp and the sea is rough. Some suffered exposure to cold and the chilling from sea-soaked clothes for many hours at a time. Tonsillitis and rhinitis were frequent and bronchitis and bronchial colds were the rule and there was also epidemic and pandemic influenza. As to dietetic indiscretions; in the destroyer flotilla on sea duty and especially in war time there is no such thing as dietary discretion. Rarely is there opportunity to eat hot or fresh cooked food, except soup and beans. The men eat standing, and hastily gulp their food. Can this predispose to gastroduodenal catarrh? In addition there is the sea-sickness, with its local pathology of a congested and erosive gastric mucosa. Now reconsider what I have just said in regard to the frequency of tonsillar, bronchial and influenzal-pneumonic infections, with the swallowing of infected material from the mouth and respiratory tract. The microorganisms are furnished and the potential etiological chain is complete. We proved nearly 100 cases of infective gastritis and duodenitis in one base hospital alone and in scores of postinfluenzal cases that I have

¹⁰ Wien, klin. Wchnschr., 1908, xxi, 189.

seen and examined since my return during the past ten months. Sixteen cases of catarrhal jaundice among these 100 is a high percentage.

Analyzing these cases I find that one occurred in a man with a pronounced oral sepsis; one in a man following intensive syphilitic treatment, oral and intravenous. Two cases occurred within a week after operations on the nose and throat, one a tonsillectomy and the other a septum repair. Four were postinfluenzal infective cases and 8 of these 16 cases occurred in men serving in the "Black Gang," that is, in the fire or engine room, below decks, where they had to swallow their infected salivary or bronchial secretions on account of naval discipline. One of these 8 cases gave a history of acute catarrhal jaundice four years previously. Possibly this case should be excluded on the ground that it was a reëxacerbation of an antecedent cholecystitis or cholangitis. But I am including it because both the histories of the first attack and the one which I observed were clearly that of simple catarrhal jaundice, and because I believe that catarrhal jaundice, simple and benign as it is, is pregnant with possibilities of future and more serious disease of the biliary tract and may prove to be a direct starting-point for some cases, perhaps more than we now realize, of cholecystitis, cholelithiasis and choledochitis. In the near future I purpose reviewing a series of catarrhal jaundice cases and to institute a "follow-up" on them to ascertain the frequency (or infrequency) of subsequent disease of the biliary apparatus.

Of these 16 cases all of them gave proved evidence of gastroduodenal catarrh plus infective gastritis, infective duodenitis or both. Nine of these cases, the first observed, were treated after the manner of the usual symptomatic or expectant plan: Bed rest; diet restricted to proteins and fats; calomel and Epsom salt courses; later other cholagogues, such as blue mass, podophyllin, aloes, etc.; sodium phosphate in hot water on the fasting morning stomach; urotropin; the salicylates or *fel bovis*; gastric lavage; during convalescence nitrohydrochloric acid and *nux vomica* or other tonics. It has been stated that cold colonic irrigations stimulate the intestinal stasis and may stimulate gall-bladder peristalsis. I have not personally tried them, but it seems to be empirical and irrational therapy. The average duration of these first 9 cases so treated was thirty-five days before the jaundice had completely cleared.

In a second group of 7 cases, because our hospital facilities were improved and because some special duodenal apparatus had arrived, I adopted the plan of treatment I now desire to advocate. At the first visit to each patient I ascertained the possibility of antecedent mouth or respiratory tract infection and then proceeded to ascertain the presence of catarrhal or infective processes in the stomach and the duodenum by examining both fasting and digesting secretions from both of these zones, chemically, microscopically and bacterio-

logically, with the help of Dr. Hugo, our pathologist. I was thus able to prove the presence not only of a gastroduodenal catarrhal inflammation but also the local implantation of pathogenic microorganisms either in the stomach or duodenum alone or at both places. Among the bacteria recovered and identifiable were streptococci, staphylococci, *Micrococcus catarrhalis* and pneumococci in both the stomach and duodenum, and in the latter bacilli of the colon group. This gave a lead as to rational treatment. All patients, whether with bronchial conditions or otherwise, were cautioned repeatedly against the swallowing of saliva; noses were sprayed with Dobell's solution; throats gargled with strong potassium permanganate solution, 1 grain to the ounce. A sterile duodenal tube was passed to the stomach in the fasting morning state, the residuum withdrawn for analysis and microscopy, with a sterile individual syringe for each patient. The stomach was washed with water, followed by liquor antisepticus alkalinus (in the hyperacid cases) or hydrochloric acid solutions (in the subacid cases), then water again until the washings were clear. Then 250 c.c. of solution, one day, of potassium permanganate (starting with one to fifteen thousand and increasing to one to eight thousand and the next day a solution of silver nitrate (one to twenty thousand to one to ten thousand) was introduced into the stomach, allowed to remain there three to five minutes, and as much as possible syringed out. The patient was then given a glass of water to drink, turned on the right side and by *slow* swallowing the tube was allowed to enter the duodenum. When this was reached (in from fifteen to forty-five minutes) the duodenal contents were aspirated for study. In all these cases the duodenum was at first found to be bile-free. So far this method of treatment is no different from the procedure to be followed for the proper diagnosis of diseases of the gall-bladder and biliary ducts. The preliminary report of this method I have published.¹¹ As was shown in that paper we utilize, clinically, for both diagnosis and treatment, an experimental method devised by Meltzer,¹² namely, to locally douche the duodenal mucosa with magnesium sulphate solution. This by local chemical or "hormonic" action serves to relax the duodenal zone, to relax Oddis's muscle, near the ampulla of Vater, and to simultaneously (or nearly so) cause the gall-bladder to compress its walls and to expel its contents. That this is actually true is capable of a successful demonstration in nearly all cases. I have had ample opportunities to convince myself of it and those who are associated with me, and those to whom the method has been demonstrated have also become convinced.

Now to return to the application of this method in treatment. After the duodenal contents have been aspirated for study I introduce through the tube 50 to 100 c.c. of 25 per cent. saturated

¹¹ Lyon, B. B. Vincent: Jour. Am. Med. Assn., September 27, 1919, lxxiii, 980-82.

¹² AM. JOUR. MED. SC., April, 1917, cliii, 469.

solution of magnesium sulphate and bathe or douche the duodenal mucosa. By connecting up the duodenal tube with a vacuum bottle (low pressure), some magnesium sulphate remaining in the duodenum is first aspirated, and shortly afterward this clear solution will be seen to be tinged yellow with bile. Later nothing but pure bile is obtained. The first bile obtained must obviously come from the common bile duct, since it is the first available source of supply. As the gall-bladder contracts and expresses its contents through the cystic duct it washes out ahead of it the common duct bile and presently we get only bile from the gall-bladder, with perhaps a few drops of added liver bile; after the gall-bladder contents have all been expelled and we continue to aspirate we recover bile freshly secreted from the liver cells and emptied into the hepatic ducts, and thence to the common duct and finally (*via* the duodenum) out into the vacuum bottle; thus, as I showed in my previous paper, we can segregate for study bile from these several sources and to differentially study them, and I sketched in that paper the type of bile seen in normal and variously diseased states. Since the publication of that paper I have recovered and identified in several instances, by cytological examination of the gall-bladder bile, columnar deeply bile-stained epithelium. This more satisfactorily proves the source of the so-called "B," or gall-bladder bile. In the treatment of this second group of 7 jaundiced cases I found that in all instances the common duct, or "A" bile, was thicker and more viscid than normal; "off color," that is, deeper molasses yellow in some cases, mustard color in others, turbid and containing much mucus in ropy, tenacious masses and much flocculent debris. Microscopically there were seen the products of catarrhal inflammations, and in one case, only, microorganisms (streptococci) were observed and later culturally proved. The gall-bladder, or "B" bile, was also found definitely "static" and off color, thicker and more viscid than normal, and several specimens contained heavy deposits of bile crystals and some microscopic catarrhal elements. No bacteria in these cases were ever found in the "B" bile specimens. In only 2 of the 7 cases was it possible to unplug the ampulla of Vater at the first treatment, but in all cases this was accomplished by the third treatment or before. Treatment should be given every day until the bile duct has first been freed and thereafter every second to fourth day, as indicated in these individual cases. Following the biliary drainage the duodenum should be disinfected with potassium permanganate or silver nitrate solutions of the same strength as used in the stomach and continued as long as the microscopic evidence of duodenitis exists. I introduce only from 100 to 200 c.c. of these solutions into the duodenum, let it remain there from three to five minutes and try then to recover what I can (often up to 50 per cent. of the amount introduced), but I have long ceased to worry about baneful effects

from that left behind, for I have seen no bad effects when $KMnO_4$ or $AgNO_3$, in the strengths up to one to ten thousand, are applied to the duodenum. Beyond this I have not tried to go, because I believe they are effective strengths. In some instances I have followed the treatment by giving a duodenal enema after the method of Jutte.

The whole description of this method of treatment and diagnosis sounds difficult and cumbersome, but it really is not so. It is true that it requires time (from one to one and a half hours), and often makes a demand on our patience as well as on our patient, but the results justify the means. And now what are the results? In the 7 cases so treated the average duration of jaundice was seventeen days and the shortest case was eleven days. Compared to the average duration of thirty-five days of the first group of patients treated by the expectant plan, this is a reduction of over 50 per cent. Not only is the duration of the disease shortened and the symptoms more promptly ameliorated, but the future dangers of damage to the biliary apparatus, from static or infected bile, from overdistended and consequently atonic gall-bladders, are to a proportional extent avoided.

I am appending a protocol of one of these cases in some detail as illustrative of the group.

Case No. XV.—W. P. A., male, aged twenty-three years. Ensign, U. S. N.

The patient had an attack of rather mild influenza on October 5, 1918 (during the epidemic). His symptoms were excessive tiredness, aching in back and leg muscles. Dull, heavy feeling in the head. Loss of appetite. Chilliness and slight fever. He had no sore-throat, but had a loose, bronchial cough, with copious purulent sputum. After several days he noticed a sense of pressure-heaviness in the epigastrium after meals, and he began to have regurgitations of food and gas odors, reminiscent of food long after he had eaten it. Several days later he noticed that his urine was becoming very dark in color.

He was first examined by me on October 11, when his chief complaint was soreness and pain in the stomach, with a sense of nausea and acute sour eructations. Gastric siphonage recovered something over 2000 c.c., sour, heavy chyme, with some food recognized as having been eaten fifteen hours earlier. Mucus, double plus. Free HCl, 7.5; total acidity, 47.5; occult blood not present.

Thorough gastric lavage given by stomach tube and Leube-Rosenheim method.

Physical Examination. Practically negative except for furred tongue, heavy breath; low blood-pressure, 104-81; enlarged area of gastric tympany after moderate air-bulb inflation and soreness over epigastrium.

October 12. Fifteen hours' fasting stomach residuum: 50 c.c., pea green, turbid, very mucoid and stringy. Free HCl, 5; total acidity, 15; occult blood, positive to benzidine, trace to guaiac. Microscopy.

Very few "food rests," starch remnants and fat globules. Much mucus. Few polymorphonuclear leukocytes, with protoplasm practically intact, considerable desquamation of endogenous epithelium; bacterial flora definitely increased; cocci and variously sized bacilli noted. Cultures planted. Fractional examination: Hyperchlorhydric curve commencing at forty-five minutes and well sustained for two and one-quarter hours, when the free HCl was 55, acidity 70 and total acidity 75. Mucus plus, no biliary regurgitation, slight motor delay. Stomach rinsed and disinfected. Tube passed into the duodenum; entered in twenty-five minutes. Duodenal contents: 9 c.c.; thick, viscid, turbid, flocculent, bile-free, with nearly 5 c.c. of granular sediment. Free HCl, 0; total acidity, 3.5; occult blood positive to B. and G. Microscopy: Mucus, plus, poorly stained necrotic debris. Many leukocytes (polymorphonuclears). Bacterial flora very noticeable; cocci and bacilli noted. Cultures planted.

October 16. Patient slightly jaundiced. Yellow sclerae and light lemon-color tint to the skin. Urine heavily bile-stained. Stool pale, pasty and fermentative. Epigastric discomfort. Gastric lavage and disinfection; mouth and nose disinfection.

October 18. Jaundice well established, of deep golden yellow. Liver dulness slightly increased. Sore to deep percussion. Stools acholic. Gastric lavage and disinfection. Duodenal disinfection with $KMNO_4$, one to ten thousand. Magnesium sulphate douche; common bile duct completely plugged and would not open. Culture made on October 12 reported: From stomach: staphylococci, streptococci, spore-bearing bacillus. From duodenum: staphylococci, streptococci, bacilli of colon group and an unidentifiable diplococcus Gram "positive, negative."

October 19. Same direct treatment of stomach and duodenum. Bile duct partially opened after magnesium sulphate, and the bile was thick, ropy, tenacious, turbid and dark mustard yellow color. Microscopically: much bile-stained epithelium emmeshed in mucus; many polymorphonuclear leukocytes, with intact protoplasm; necrotic, poorly staining debris; bile crystals; bacteria plus; bacilli and cocci; some definitely arranged in chain formation. From now on the following treatment was practised: Gastric and duodenal lavage and disinfection using potassium permanganate in increasing strengths, magnesium sulphate douche and biliary drainage on October 21, 25, 30 and November 7, and the same plan, only substituting silver nitrate disinfection, on October 23, 28, November 1 and 4.

October 25. The jaundice has completely disappeared. The urine was normal. The stools were normal. The patient's appetite has returned and he has more ambition and "punch." Duration of jaundice eleven days.

November 4. Smears from the duodenum showed: A very striking diminution in the bacterial flora; no polymorphonuclear

leukocytes were observed; no necrotic debris. Occult blood was negative.

November 8. The patient was discharged to duty.

The protocol of this patient was very little different from the others, and was selected because it illustrated the method and its results. Finally, I desire to state that this protocol was made up from the original notes and was not reconstructed from memory.

THE OCCURRENCE OF HYPOCHLORHYDRIA IN GALL-BLADDER DISEASE.¹

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LESS than a decade ago, chronic surgical indigestion began to be recognized, the principal causes being gastric and duodenal ulcers, gall-stones and chronic appendicitis.

The train of symptoms—pain, nausea, distention, eructations, and pyrosis—is said to be due to pylorospasm and this in turn to an increase of hydrochloric acid in the stomach. The most modern authors speak of pylorospasm as the result of hyperacidity, frequently of neurotic origin, but warn that organic gastric conditions and extragastric lesions must not be overlooked. In the discussion of nervous gastropathies in *Modern Clinical Medicine*, while referring to the neurotic and dietetic indiscretions as a cause, it is stated: "Take care not to overlook gastric and duodenal ulcers or reflex causes of hyperacidity, such as cholelithiasis, chronic appendicitis and ileal stasis." The same volume under symptoms of gall-stones mentions reflex disturbance of the stomach (hyperacidity).

Kaufman, in Forchheimer's *Therapeutics*, says that hypersecretion and pylorospasm are closely interlocked, that next to gastric and duodenal ulcers, gall-stones and chronic appendicitis are the most frequent centers of irritation and causes of the irritating gastric disorder. He thinks that hyperchlorhydria is likely the cause of ulcer, gall-stones and appendicitis, the increased acid being due to some underlying condition causing irritation of the vagus nerve.

Moynihan,² in discussing hyperchlorhydria and ulcer says: "Hyperchlorhydria is present in other diseases, notably cholelithiasis and appendicitis, and its presence possibly explains the mimicry of the symptoms of ulcer by these various diseases."

One might continue quoting others along this line almost indefinitely, for the recent literature contains innumerable papers supporting gastric disorders in gall-bladder disease as due to hyperacidity.

¹ Read at Richmond Surgical Society, April 2, 1918.

² *Lancet*, January 6, 1912, p. 9.

I wish to present the following report of gastric findings in 61 cases of bile-tract infection, with and without stones, proved at operation, which I have had the opportunity of studying at St. Luke's Hospital. The total number of gall-bladder cases recorded is about 700, but unfortunately in the majority of instances a gastric analysis was not made. In some patients the disease was found during the course of operation for other abdominal conditions, in others the history, symptoms, and physical findings made the diagnosis clear and the patients were not subjected to the stomach-tube. In the cases reported the Ewald test-meal was used, the free and combined acids estimated by titration with one-tenth normal sodium hydroxide after the addition of Topfer's reagent and phenolphthalein. The analyses were made by a most competent pathologist, Dr. E. Guy Hopkins.

Of these 61 cases 16 show an absence of free HCl, 45 show free HCl, of less than 20, 11 come in the bounds of normal and only 5 cases show an increase of free HCl. Referring to the total acidity we find 11 cases showing a total acidity of 50 or more and 39 show a total acidity of less than 40. No cases have been included that show any associated organic stomach condition, cancer or ulcer, or malignancy of the gall-bladder or pancreas.

While the findings reported are different from previous teaching we are not alone in our observations, for there is an increasing number of articles appearing in which the authors find a low percentage of hydrochloric acid in gall-bladder disease.

Hohlweg³ states that hypochlorhydria is an important sign of gall-bladder disease occurring in from 71 to 84 per cent. of cases.

V. Aldor⁴ found in 61 per cent. of his cases either normal acidity or subacidity. His article is abstracted in *Progressive Medicine* (December, 1914), and the reviewer states that his figures are at variance with the view generally held, namely, that hyperacidity is the rule.

Olly⁵ reports 87 cases of uncomplicated gall-stone disease and found that in the great majority of cases hypo-acidity is the rule.

Hernando⁶ calls attention to the high percentage of cases showing gastric anacidity.

Wohl⁷ reports that more than half his cases show a great diminution or absence of hydrochloric acid.

Hamburger,⁸ in discussing subacidity, gives as one of its causes gall-bladder disease.

From the number of cases that we report, and from the limited evidence from other observers, compared to the vast literature that

³ Deutsch. Arch. f. klin. Med., 1912, cviii, 255.

⁴ Wien. klin. Wehnschr., 1914, No. 18.

⁵ Arch. f. Verdkrank., 1915, xxi, 128.

⁶ Arch. des mal. l'App. Dig., 1914, p. 274.

⁷ New York Med. Jour., February 24, 1912, p. 347.

⁸ Med. Clinics of Chicago, January, 1917.

Case No.	Free HCl.	Total acidity.	Operative findings.
1	4	44	Cholecystitis.
2	14	26	"
3	6	20	"
4	24	58	"
5	6	30	"
6	0	10	"
7	45	65	"
8	15	65	"
9	10	38	"
10	17	33	"
11	11	26	"
12	10	45	"
13	8	80	" with stones.
14	22	48	" "
15	0	18	" "
16	32	56	" "
17	22	45	" "
18	14	22	" "
19	18	36	" "
20	29	49	" "
21	0	14	" "
22	0	11	" "
23	5	20	" "
24	9	35	" "
25	30	50	" "
26	0	16	" "
27	6	35	" "
28	35	46	" "
29	20	58	" "
30	10	38	" "
31	0	14	" "
32	6	16	" "
33	6	29	" "
34	25	34	" "
35	4	24	" "
36	20	47	" "
37	0	12	" "
38	11	40	" "
39	0	9	" "
40	10	50	" "
41	0	5	" "
42	20	30	" "
43	15	40	" "
44	0	24	" "
45	0	36	" "
46	10	36	" "
47	0	8	" "
48	0	6	" "
49	10	15	" "
50	40	62	" "
51	40	51	" "
52	0	40	" "
53	17	39	" "
54	0	10	" "
55	10	18	" "
56	5	22	" "
57	18	58	" "
58	0	4	" "
59	20	42	" "
60	12	28	" "
61	20	39	" "

finds hyperacidity the rule, we do not think we have undisputed evidence, but this has been our experience, and we look for a cause of the low acid secretion as well as an explanation of the digestive symptoms.

Hypo-acidity may be the result of loss of a hormone that is secreted by the normal gall-bladder, which loss inhibits the secretion of hydrochloric acid, or it may be due to a disturbance of intermediate chloride metabolism.

There may be several factors, either separately or combined, which contribute to the gastric symptoms. Eructation, accumulation of gas, oppression, fulness after eating, pyrosis and such common digestive symptoms are as likely to be found with diminished acidity as in overproduction.

We believe with Hamburger that the pain in these conditions, as in gastric and duodenal ulcer, is due to the increased intragastric pressure. He has shown that pain occurs coincident with increased intragastric pressure in stomachs in which there is a complete absence of acids.

Pylorospasm, which has so often been the explanation of reflex gastric pain, may be the cause of increased intragastric tension and may occur in cases of subacidity.

A review of the normal action of the pylorus is necessary when one claims anything so radically different from the usual teaching. Cannon and others have shown that when food is taken into the stomach the pylorus almost immediately opens and some food passes out into the duodenum. The presence of this acid chyme in the duodenum causes closure of the pylorus, which does not open again until the acid is all neutralized by the alkaline duodenal contents. Pylorospasm is the almost continuous contraction of the pylorus, said to be and in most cases is due to increased acid secretion. But after all it is only a relative disproportion of acid to alkali, and if some day we find that in bile-tract infection there is a low alkali percentage in the duodenum, the same disproportion of acid to alkali would exist even though the acid were diminished, and pylorospasm would be the result.

Another cause for the gastric symptoms may be due to spasm caused by irritation from disease. Physiologists have shown that irritation in one part of the intestinal tract causes spasm in the region above, so the natural place for contraction spasm from gall-bladder disease would be the pylorus irrespective of the amount of acid.

One of the most frequent gastric symptoms that we have noticed is the accumulation of gas in the stomach. The oppression caused thereby and the eructation in the light of our findings is attributable to poor digestion of proteids and the consequent fermentation.

Along with this observation of hypo-acidity in gall-bladder disease would naturally arise the question of cholecystectomies as a routine procedure in all cases of gall-bladder affections. Whether

the gall-bladder has a function or not and the effect of its removal must be decided before we can dogmatically say that all diseased gall-bladders should be removed.

Hohlweg⁹ made the observation which is not at all new that patients who have undergone operation for the removal of the gall-bladder not infrequently return with gastric symptoms. He had the unusual opportunity of studying 42 cases and was astonished at the hydrochloric acid deficiency in 83.3 per cent. He was able to show that a similar phenomenon could be produced in dogs after cholecystectomy.

Kemp demonstrated that there is a difference in the alkalinity of the bile before and after it enters the gall-bladder, showing that the gall-bladder must have some function.

Rost found that animals without gall-bladders secreted only one-third as much bile and pancreatic juice as animals with gall-bladders, even though normal stomach contents were injected into the duodenum. He believes this is due to the lowered production of secretin, as it could not be due to the reduction of hydrochloric acid.

Ohly, quoted by Leede in *Northwest Medicine*, found that after loss of the gall-bladder 70 to 80 per cent. of cases showed anacidity and achylia gastrica. In a series of 39 cases of this type 71 per cent. showed lack of free HCl, 17 per cent. showed free HCl below 20 and 12 per cent. were normal.

In another series of 45 cases in which stone-occlusion of the cystic duct or strong shrinkage of the gall-bladder was found, 84 per cent. showed no free HCl, and 14 per cent. were below normal.

The deductions of Leede are that any condition that brings about loss of function of the gall-bladder disturbs the secretion of the hydrochloric acid, with more or less disastrous results to the patient.

Many observers have noted the attempt on the part of the bile ducts to dilate and form, as it were, a new gall-bladder so far as the intermittent flow of bile is concerned.

The loss of a hormone is taken up by Leede. He believes that possibly a hormone is secreted by the gall-bladder which causes the secretion of HCl in the stomach, the acid chyme passing into the duodenum, causing the production of secretion, and this in turn acting on cells of the liver and pancreas, causing a production of their respective juices.

To go further into the surgery of the gall-bladder is entirely out of the province of this paper, which is primarily a report of gall-bladder cases that show gastric subacidity in the vast majority. It would seem in passing, however, that if we are anyway nearly right the proper procedure in gall-bladder surgery would be to study the function of the gall-bladder, using the acid produced in the

stomach as an index to the remaining function of the gall-bladder and preserve all those that seem capable of functioning.

In conclusion we must remember the inaccuracy of a single stomach analysis in individual cases, also that fractional analysis is far superior, a procedure we propose to carry out in another series of gall-bladder cases. However, much importance should be placed on the high percentage of cases in such a series that show hypo-acidity.

THE TREATMENT OF HYPERTENSION.

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IN a previous paper¹ I discussed the relationship of hypertension to arteriosclerosis and nephritis and described a "type" individual in whom hypertension and hypertensive states are commonly found. I predicated the conception of hypertension as a primary pathological physiological state, due to unknown causes, and that arteriosclerosis and nephritis were not primary but secondary manifestations, consequent to the hypertension itself or to the cause or causes of the hypertension. In this conception, hypertensive states are subject to the same laws of circulatory dynamics as other cardiovascular disorders (*e. g.*, valvular heart disease) and have the same compensated and decompensated phases. I also tried to show that persistent hypertension represents a progressive process; that in all probability most hypertensive states begin as cases of "essential" hypertension, and that unless complicating factors are introduced such cases eventually develop the graver evidences of cardiac and renal insufficiency, affording the clinical picture of arteriosclerosis, coronary disease, chronic nephritis, etc. I also tried to emphasize the lack of relationship between the clinical and laboratory findings in hypertensive states and pathological anatomy, and attempted to show that many of the clinical phases of hypertensive states (especially nephritis) have no predictable pathological substratum, as far as "type" kidney is concerned.

The "type" individual that I have described is a combination of both physical and psychical characters. Briefly, these individuals are overweight, have short necks and are slow and unathletic in bodily movement. Psychically they may be described as prematurely old. They lack the ability to play, either mentally or physically; their imaginations are stunted, their mental range is narrow, but within its limits terribly intense. As their moments of relaxation are few they burn up their energies swiftly, until at

¹ AM. JOUR. MED. SC., November, 1919.

middle age they are exhausted, and the rest of their life is spent in seeking health. To my mind the states associated with hypertension are essentially by-products of the struggle for existence, the ultimate consequences of "the strenuous life."

With these theses in mind I shall discuss the treatment of hypertension under the following headings in the order of their importance: 1. Instruction of the Patient. 2. Reduction Diet. 3. Exercise and play. 4. Drugs.

1. INSTRUCTION OF THE PATIENT. "Blood-pressure" in the minds of most patients is synonymous with apoplexy and Bright's disease, and it is only too true that many patients on being told that they have increased blood-pressure promptly become confirmed hypochondriacs. Every trivial symptom henceforth is ascribed to the "blood-pressure" and is magnified to the nth degree. The patient becomes morbid, irritable, introspective and becomes a pitiable subject of that mental anguish termed "anxiety neurosis." Such patients would have been better off had they been told nothing.

Extreme tact is therefore necessary in imparting the status of things to the patient. The significance of the malady must be minimized to the utmost. It is important to gauge the temperament of the patient carefully and no more or less should be told than is sufficient to make the patient realize the necessity of following instructions. The best *rapprochement* between physician and patient will be obtained, I believe, by a tactful explanation of the nature and significance of hypertension. Here, as in every other relation between physician and patient, the doctor should be a teacher, as well as a healer.

The advice so lightly and so frequently given, that patients with hypertension should "retire" from business, I deem especially pernicious. The rapid aging of patients after "retirement" is altogether too common an observation not to be taken seriously. I do not know who it was who said that it is the triad—work, play and a sense of responsibility that keeps people mentally young. When these things are suddenly taken away there comes an "early and crabbed age." The advice to retire would not be so bad if an attempt were made to substitute another variety of mental occupation, but, as a rule, no such attempt is made. The consequence is that these poor souls wobble in space and have no anchorage to existence except their illness. Their main occupation thenceforth becomes the elusive quest for health.

For these reasons I advise such patients to stick to their work. In some cases it may be necessary to shorten the hours or to devolve some of the details of the business upon other shoulders. New ventures or vast expansions are prohibited. Occasionally, if the business is not entirely congenial, new lines of replacement activity are suggested, such as work in charity or social service or the culti-

vation of a hobby. Whatever activity is advised it must be something which will give pleasure. An uncongenial task is worse than none at all.

These patients must also be instructed in the very great value of holidays. Holidays are of value not only because they furnish the element of change but also because they afford opportunity to derive new mental impressions and a fresh viewpoint.

2. DIET. The diets that have been recommended for hypertensive states are numerous and various. Most of them revolve around the principle that the protein must be cut to a minimum. As far as I can see a low protein diet for hypertensive states is simply a therapeutic legacy, unfounded on any experimental or empiric evidence. A high protein diet, especially of meats, was considered bad because the split proteins resulting from digestion were supposed to injure the kidney epithelium, damage the blood-vessels, increase the albumin, and thereby bring about a quicker dissolution. I know of no evidence, either clinical or experimental, that unqualifiedly prove these things. Epstein deserves great credit in having shown experimentally and therapeutically that in one type of kidney disease characterized by large quantities of albumin and edema which he terms "parenchymatous nephritis," a high protein diet not only makes the edema disappear but often even cures the malady itself, despite the high retention of non-nitrogenous products in the blood. I have never seen that a high protein diet influences either the quantity of albumin or the hypertension in hypertensive states.

These patients, as I have said, are overweight, due to overeating, lack of exercise and often alcohol.

As the result of my observations I am convinced that the conventional tables for normal weight in proportion to height are altogether too high. As in diabetes, where Allen has shown that patients do better and show a higher tolerance when the weight is reduced to a certain limit, so in hypertension it will be found that, other things being equal, both the subjective and objective improvement will be found to be at their maximum when the patient has reached a certain weight, usually lower than that which these tables prescribe. This weight should be determined in each individual instance, and it will, as a rule, usually be found that an increase in weight, sometimes only of a few pounds, is attended by an aggravation of both the subjective and objective phenomena. In this sense it is necessary to determine a threshold, as in diabetes.

The diet that is ordered is, in many respects, similar to that of a case of diabetes of fair tolerance. The diet is simple and consists principally of fruit, coffee or tea (without sugar), meat, green vegetables, salad, cheese and a limited quantity of bread. In other respects the quantity is not limited. Indeed, there is no reason why these patients should suffer hunger. When a minimum weight is

reached a further loss may be prevented by slowly adding food of higher caloric value. Alcohol is excluded simply because a good reduction cure is impossible with it. I fully agree with Cabot that alcohol has no direct influence upon hypertension or hypertensive states.

3. EXERCISE. I feel convinced that the term "rest" is the most pernicious that can be given to patients with a compensated hypertension. The fear that exercise puts a strain on the heart, and that it increases the so-called noxious products of metabolism, I have proved to my own satisfaction to be unfounded. Rest, it is true, plays a large part in the treatment of hypertension, but only in the periods of circulatory insufficiency and under certain conditions which I shall specify. But patients with hypertension in a state of compensation, no matter what the state of disordered kidney function may be, stand exercise remarkably well. Of course the amount of exercise must be graduated, and the transition from the state of lethargy to that of heightened activity must not be too sudden. It is important that it be systematic. Exercise taken capriciously is not of much avail.

The ideal form of exercise for patients with hypertension is golf. The advantages are many: (a) It is the least strenuous of outdoor sports. (b) It involves a large amount of walking without seeming effort. (c) It is a play and not a task. (d) It generates a sporting instinct, which is reflected in their mental attitude to the problems of life.

If for various reasons a sport cannot be undertaken, walking provides an excellent means of exercise. No specified number of miles is ordered; the patient is told to walk until he is tired; this varies from three to five miles a day. It should be brisk, uninterrupted and done daily. It is remarkable to see how much further a patient can walk than he formerly felt himself capable.

If for one reason or another even walking is not possible, systematic brisk massage will serve up to a certain point as a tolerable substitute for exercise.

The effect of exercise in hypertensive states furnishes another analogy to diabetes. As Allen has shown that exercise increased the tolerance of diabetics, so in hypertension the tolerance, in terms of efficiency, is increased.

The attainment of the minimum weight alone, by diet and exercise, has a truly remarkable effect in cases of compensated hypertension. Their wind is better; their aches disappear; their cardiac reserve increases; they no longer are perpetually tired; their movements are quicker; they sleep better; they are livelier mentally; in a word they become more efficient individuals. Objectively the pulse is slower; slight irregularities, probably due to extrasystoles, disappear. The effect on the blood-pressure is peculiar. The systolic pressure is lowered, but not nearly to the

extent of the diastolic, so that the pulse-pressure is increased, sometimes quite markedly.

There is nothing more hazardous than to try to judge the condition of the patient by the amount of decrease of the systolic pressure; the patient's improvement may be decided, although the systolic pressure remains where it was or is only slightly decreased. A more accurate measure of improvement is in the decrease in diastolic pressure and consequent rise in pulse-pressure. Subjective improvement more nearly goes hand in hand with a decrease in diastolic pressure and a rise in pulse-pressure, and this nearly always is accompanied by a slowing of the pulse. The significance of the slowing of the pulse will be discussed under the heading of "drug treatment." As Goepp correctly observes, it is the ratio and not the height of the pressure that determines prognosis and connotes improvement.

The improvement in circulatory pressures is accompanied by greater diuresis and diminution or even disappearance of the albumin.

Possibility of Cure. There is no doubt in my experience that the earlier the patient is seen the nearer to normal the patient can be brought by simple reduction cures. And here I venture to set forth an observation of profound importance: It has often been questioned whether a patient with persistent hypertension can ever be brought back to normal. Most authorities deny that this is possible. But I have met with perhaps a dozen or more instances in which I believe a complete cure has been effected. I mean by that that the blood-pressure has receded to normal limits; the urine has been completely freed from albumin and casts, the heart action is normal and all subjective phenomena, such as dyspnea on exertion, headaches, vertigo, palpitation, have completely disappeared. It is possible that in subsequent years something may yet develop, but thus far the patients are, for all practical purposes, well. All the patients, so far as I can recall, were early cases. The pressures were not high: the systolic varied between 150 Hg. and 170 Hg.; the diastolic was only slightly over 100; the urine showed only a faint trace of albumin and the pulse was not much increased in frequency. The amount of overweight seemed to have had no bearing. I recall one patient who was almost obese.

Rest. As I have said, rest plays an important part in the treatment of hypertension. It has three indications: (a) In severe circulatory insufficiencies as revealed by a rapid and irregular heart, hypostatic congestions, oligurias, with marked increase in albumin, edema of the lungs, uremias, dropsy, cerebral manifestations, etc. Here the indications are precisely those of decompensated valvular lesions. (b) In cases of so-called "essential" hypertension, with high systolic and diastolic pressures, a full bounding pulse and accompanied by signs of premonitory cerebral hemorrhage. It is remarkable that the brain seems to be a *locus minoris resistentiæ*,

even when the heart and kidney show no pronounced aggravation of signs. (c) In cases of long-standing hypertension, with marked aggravations of all the focal organic signs, with severe dyspnea and general enfeeblement. In these patients, of necessity, the enforcement of an active life would be cruel. Such patients also, I have found, gladly take to the idea of spending one entire day of every week in bed.

4. DRUG TREATMENT. The main desideratum in the treatment of hypertension is, as I have shown, the maintenance of the best possible circulatory function; in other words, to try, if possible, to place the circulatory function in the condition of so-called "compensation." Attempts to reduce the blood-pressure by direct methods long ago have been proved futile. We have drugs that reduce blood-pressure, but their effect is evanescent and no permanent gain is ever derived. With the aid of the therapeutic means I have described, either alone or with the aid of drugs, we do effect lasting decreases in blood-pressure, but these are entirely secondary. It is entirely possible to bring about vast subjective and objective improvement without appreciable effects upon the blood-pressure, nor is this improvement, as I have shown, always proportional to the decreases in pressure. As in valvular and muscular defects of the heart the main drug upon which we rely to maintain a correct circulatory balance is *digitalis*. For many years *digitalis* was contraindicated in hypertension, because it was supposed to increase blood-pressure, by increasing the power of the muscle and contracting the peripheral bloodvessels. It was therefore considered *the* heart stimulant *par excellence*. We know that *digitalis* in the normal heart at all events never directly increases the blood-pressure, except in doses that are far beyond the therapeutic maximum. In recent years the opinion is gaining ground that the main effect of *digitalis* is expended in affecting the rhythm of the heart. It affects irregular hearts more than the regular; it makes irregular hearts regular and it slows regular hearts to a limited extent. In irregular hearts, as in auricular fibrillation, *digitalis*, it is true, increases the blood-pressure, but the effect is entirely secondary and conditional upon the improvement in the rhythm. It would lead me too far to discuss the therapeutic indications of *digitalis* in general, but I may say that my conception of *digitalis* is that of a regulator and not that of a "stimulant." It may be aptly likened to the timer of an automobile engine.

With the clearer understanding of the effects of *digitalis* our timidity as regards its employment in hypertension has completely disappeared. Its indications in decompensated states of hypertension with the signs and symptoms which I have outlined already are obvious. In such instances the heart is rapid and usually irregular and the effect, except in cases where the decompensation has gone too far and the reserve force of the heart has been lost,

is almost magical. These patients are the so-called "cardionephritides." When all signs of decompensation have disappeared, the principle consists in keeping the heart at a certain rate by the continuous use of digitalis. Each patient must be studied with this end in view, and eventually a rate will be found in which the patient's condition both subjectively and objectively, will be at its best.

But the value of and the indications for digitalis in compensated cases of hypertension have not been generally appreciated. This is a subject worthy of extensive study. I know of the therapeutic benefits that may be obtained, but I am not at all clear as to what physiological forces or agencies these benefits may be ascribed. I can best describe what I mean by citing a concrete example. A patient complains of slight shortness of breath on exertion, pains (very often anginoid) about the precordium and headache or vertigo. An increased blood-pressure is found, a pulse only moderately rapid, between 80 and 90, and perfectly regular; the urine is lessened in amount and contains albumin and casts. Place this patient upon full doses of digitalis and the symptoms disappear, the quantity of urine increases and the albumin decreases; the systolic pressure decreases only a few points, the diastolic pressure a little more. The pulse-rate at rest, however, comes down a varying number of points, from only 4 or 6 to perhaps 10 or 20, depending on the original rate. Now comes the interesting fact: if such a patient is kept at this rate of heart action he will remain well and all the other objective signs, such as the blood-pressure and the condition of the urine, will be found to remain constant. When the pulse at rest remains persistently above this rate the patient will invariably be found to be worse. This rate may be as low as 60 or as high as 90. Individualization of dosage is therefore a paramount necessity.

Why digitalis causes such pronounced improvement I am at a loss to explain. Whether the effect is entirely due to the slowing of the heart, enabling the organ to accumulate a greater reserve force in diastole; whether it increases the velocity of volume flow or whether it improves the coronary circulation, I do not know. But the fact that digitalis is a "real drug" in the treatment of apparently compensated cases of hypertension, as well as those that are decompensated, is to my mind an incontrovertible fact. Its administration requires judicious study and furnishes an abundant field for clinical and experimental investigation.

Digitalis is, of course, useless in cases of hypertension, with a constantly slow pulse (around 60). But a pulse of 74 or 80 need not be considered a contra-indication for its use.

Nitrites. The drugs of the nitrite group introduced by Lauder Brunton unquestionably diminish blood-pressure, but the effect is transient. These drugs have, nevertheless, a definite field of usefulness, but only, I believe, as symptomatic remedies. They unques-

tionably relieve what have been termed "spasm" phenomena, such as anginoid attacks, transient aphasias, numbness and paretic symptoms due to cortical irritation, headaches and vertigo. I think most of us have seen patients in whom nitrites, when first administered, cause a temporary increase in headaches. I believe it is a mistake to stop the drug for this reason because I have found that if persisted in the headaches will disappear. If nitrites are given the dose must be given frequently rather than, as usually done, three or four times daily.

Iodides. The use of iodides in hypertension was based upon the theory that arteriosclerosis caused hypertension and that the iodide compounds softened the sclerotic vessels and so reduced the tension. Inasmuch as the testimony is overwhelmingly in favor of arteriosclerosis being secondary to the hypertension, and that, furthermore, the iodides cause no appreciable softening of the blood-vessels except perhaps in syphilitic instances, this theory, therefore, lacks support. The advocates of iodide therapy cling to the more recently promulgated theory that these drugs do good because they change the osmotic tension of the blood. But I have found no evidence that they do. At all events in frank hypertensive states I have never been able to convince myself that I have accomplished anything and have therefore practically abandoned their use. The only occasions in which I still employ them are in patients with hypertension with an old history of syphilis and who complain of persistent headache. In such instances it acts better than any other therapeutic measure.

Chloral Hydrate. Small doses of chloral hydrate repeated over a long time do unquestionably reduce the blood-pressure, but I believe chloral produces this effect by its sedative action alone, just as morphin will. Patients with hypertension are liable to be "nervous" and are poor sleepers, and I question, therefore, whether chloral acts better in such cases than any of the milder sedatives and hypnotics. My observations lead me to believe that patients with hypertension need their full quota of sleep.

Caffein. The view is now generally held that the various caffein salts are pure diuretics and that their effects on the heart are practically negligible. These caffein salts do improve conditions associated with hypertension only in so far as they lessen the embarrassment of the heart by lessening the fluid content of the body. These salts are therefore eminently useful in the decompensated states of hypertension.

THE MEDICAL TREATMENT OF AORTIC ANEURYSM.

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THE purpose of this article is to emphasize the necessity and value of medical treatment in a condition which too often is regarded as hopeless from the point of view of therapy. The aneurysms under discussion are of the thoracic aorta, and have as their etiological background the disease syphilis. One does not, however, wish to convey the impression that syphilis is the only cause of aortic aneurysm. We have in the pathological museum at the medical school two really beautiful specimens of mycotic aneurysm of the ascending aorta of known *Streptococcus salivarius* etiology. These have been reported by Klotz, but this is the exception while syphilis is the rule. The relation of syphilis to thoracic aneurysm has been so clearly shown by clinical, serological and pathological workers that one is not surprised at finding the two conditions, in fact, really one disease, together in almost 90 per cent. of the reported cases. We do not refer in this article to aneurysms in which this relationship cannot be demonstrated.

It is advantageous to recall, briefly, the lesion produced in the wall of the aorta by the *Spirocheta pallida*. The nature of the process is well established, and in practically all of the text-books of pathology it is minutely described. We would, however, refer the reader to Longcope's article, which discusses this subject in a very complete way. Syphilis produces in the wall of the aorta a granulomatous inflammation extending from the adventitia into the media and intima. The perivascular channels about the vasa vasorum of the outer two coats appear to be the road along which the spirochete passes, and it is well to keep in mind that this organism has been found in all of the layers of the aorta. Hence the presence of granulomatous tissue in any portion of the wall is to be expected. The media and adventitia show the greatest inflammatory reaction. The destruction of the media, composed as it is chiefly of elastic fibers, is considerable, the amount depending on the severity of the process. This naturally leads to weakening of the wall, and nature attempts repair by laying down fibrous tissue, the contraction of which in part gives a peculiar characteristic wrinkling to the intima, which is so valuable a sign in the gross diagnosis of syphilitic aortitis. The adventitial reaction is of the same type, but here one sees more connective-tissue change and more marked perivascular infiltration of lymphoid and plasma cells. Patchy intimal thickening is very evident.

Further, and of considerable importance, is the variable amount of gummy necrosis in the wall. From a pathological point of view

there is really no difference, save one of degree, in the inflammatory process of a syphilitic aortitis, with or without aneurysm. We have never seen an aneurysm which came to autopsy that did not show evidence of gummy necrosis in its wall, at times seen only microscopically, but often apparent in the gross. In this connection the report of Winternitz is of considerable value. He was able to observe the development of a very early aneurysm in a young syphilitic negro woman dying from coronary thrombosis. He could follow the granulomatous inflammation from the adventitia inward through the media, which was locally destroyed, and see a pouching of the intima into this area. This case, Winternitz, believes confirms Benda's view that the development of aneurysm is secondary to inflammation and necrosis of the wall and not a gradual stretching of the fibrous tissue, which replaced these necrotic areas in the process of repair or healing. We agree with this view. Aneurysm, as we are using the term, really means a chronic progressive and active syphilis of the aortic wall, hence our therapy must be in accord with this picture if we are to expect good results. That is only logical.

That the fibrous tissue areas representing healed lesions seen in the wall of a syphilitic aorta or an aneurysm lying between the ruptured elastic tissue fibers stretch under the constant pressure is most likely, but we do not feel that this plays a part of any importance in the actual production of the lesion; further, it seems to us as most improbable that the rupture of an aneurysm is ever due to the breaking or giving way of this fibrous tissue. In this connection we wish to refer to the work of one of our colleagues, Dr. C. C. Guthrie. The dog on which he did his first arterial transplantation, eleven years ago, died this past winter from a malignant tumor, with general metastasis. The transplant in the carotid was, of course, the point of interest. This was represented by a dilatation about the size and shape of a large hickory nut. This dilatation Dr. Guthrie had observed several months after the original operation, so he could definitely say that it had been present for at least ten and a half years. The wall of the dilated portion shows fibrous tissue plus the calcified remains of the transplant, with no ingrowth of muscle or elastic tissue from the adjacent carotid artery and no cellular inflammatory reaction. Here we have an example of a fibrous-tissue wall of an artery, with nothing to indicate that rupture was even impending, functioning for over ten years and in gross structure a true aneurysmal sac. The point brought out by Guthrie's experiment, which is to us of value in the localized sense of our present discussion, is that fibrous tissue can act as a vessel wall and not rupture for a period of many years, in this case lasting the lease of life of the animal. It is very probable, however, if an inflammation of any type had developed in the wall of this sac the result would have been a ruptured aneurysm. This experiment

also shows, as indicated above, that fibrous tissue may be stretched in a vessel wall to assume a sac-like appearance, but the conditions underlying the change here are entirely different from those met with in the human aorta. In man the cardinal point is an active inflammation. If we could succeed in stopping entirely this inflammatory reaction and produce healing by fibrous tissue replacement, which we know occurs then, it would be possible, by analogy, to compare this very interesting animal work with our clinical problem, particularly in reference to the prognosis.

It would seem therefore rational that the therapy of aneurysm should be directed primarily against the spirochete with the idea of its destruction, which would be followed by the eventual absorption of the inflammatory process in the wall of the vessel and the subsequent replacement fibrosis or healing. The results would depend a great deal upon the amount of damage done and how thoroughly we are able to sterilize the areas infected by the spirochete. Assuming that this latter condition is a possibility, does it not suggest a more favorable outlook for these cases? The fact that an occasional spontaneously healed aneurysm is met with, certainly seems to indicate that an enlarged thoracic aorta, if quiescent, is compatible with life. From some limited observations on aortic aneurysm during the past three years we feel that the condition is by no means as hopeless as is ordinarily considered.

The prognosis of this lesion has always been very poor. It is well known that a certain number heal spontaneously. They are met with occasionally at autopsy. On the whole, however, this fortunate group is not very large and there are probably very few physicians who have clinically diagnosed aneurysm and who have seen a so-called spontaneous cure on the same patient. Osler gives almost a hopeless outlook, but calls attention to the fact that some even unusually large aneurysms have been known to last for many years. These, he says, are not common. Of the majority, after the diagnosis has been made, a period of one or two years usually sees the end. Excepting the unusual case one would be correct in saying that thoracic aneurysm is a fatal condition in a relatively short period of time after symptoms develop. This is the consensus of opinion as given in the modern text-books and other literature.

The commonest cause of death is rupture of the sac. This rupture, we believe, is due to the giving way of the necrotic and inflammatory tissue in the wall of the sac and not the breaking or tearing of fibrous tissue which represents healed portions of the wall. Fifty-three per cent. of the 1829 cases referred to by Arnold died of rupture. Cardiac failure from myocardial and aortic valve disease, angina pectoris, asphyxia, edema of lung, hypostatic pneumonia, tuberculosis or other intercurrent infections make up the rest of the list. Even if the death is not due to rupture of the sac most of the other causes are more or less directly dependent on this

large mediastinal mass. The aneurysm itself is therefore directly or indirectly responsible for the great majority of the deaths from this condition.

The medical treatment of aneurysm, as judged by past clinical experience, has not been brilliant in its results. There is always a fatalistic touch to what is written on this part of the subject. At the best the most one appears to be able to do is to relieve untoward symptoms temporarily, particularly if the lesion is at all advanced. Most authors speak of the use of mercury in those cases in which the luetic infection is known to be of a relatively recent date or where the aneurysm is supposedly small. The use of mercury, however, is not emphasized but rather gives one the impression of being suggested *en passant*. Certainly it is not brought out with the same force that one indicates when referring to tertiary lues of almost any other source. Potassium iodide, on the other hand, has been the drug of this condition for many years. It is astounding to note how often this drug alone is given in aneurysm, when with any other tertiary luetic lesion the solitary use of iodide would be considered an inexcusable error, as it is the general belief that potassium iodide, although having great power in stimulating absorption of the syphilitic process, does not kill the *Spirocheta pallida* and hence does not reach the cause of the disease. We cannot help but feel that in the treatment of aneurysm not enough attention has been focussed on the inflammatory lesion in the wall of the aorta. It is here that the cause is to be met, and it does seem rather futile to hope for results if we do not try to render the aortic wall free from the infection. As far as we know mercury and arsphenamin preparations are the only ones capable of destroying the spirochete. The cardinal principle then in the treatment in which we are striving for a possible cure in the early cases or for palliative effects in the late is to deal with the process as a syphilitic one and to apply, as fervently as possible, antisyphilitic remedies. Let us attempt to heal the inflammatory lesion in the wall and trust to the patient to fill up the sac with a fibrin clot. There are several points to be observed in the treatment which it would be well to briefly enumerate.

1. REST. As soon as the diagnosis is made the patient should be put to bed and kept there for as close to three months as possible. We allow them to get up to go to the toilet. As has been pointed out by Osler, many aneurysms will become symptomless on this rest alone. It is of the greatest value, and any treatment that does not take into account a prolonged rest in bed is falling far short of the ideal. Following the period of almost absolute rest, for the remainder of the year the patient should be limited in his physical work. We do not consider it wise to eliminate all activity, for, as a matter of fact, very few people are financially or mentally able to withstand a year of complete idleness. Undue exertion, worry and extra mental effort are to be avoided and this should more or less

be the basis for the remainder of the patient's life. It has been our experience, however, to deal with patients that were unable to take more than six weeks' rest, and following this go back to their former occupations. A change of occupation to something less strenuous is always advisable. We believe it is a good thing in many ways to have the individual kept moderately busy, as this is the best way to eliminate worry.

2. DIET. The old treatment was more or less based on diet and rest. Valsalva rested, starved and bled the patients. It must have been a very rigorous case which survived, and probably the remark that the cure was as bad as the disease was more or less true. This form of treatment was supposed to put the patient in so low a condition that the blood-pressure on the aneurysm would be greatly reduced, also possibly the coagulation or fibrin formation in the sac would be increased. The first part undoubtedly was attained. Osler recommends bleeding as an emergency measure, particularly for some severe cases of dyspnea. We have seen one case given considerable relief by this procedure. Bleeding was a very important part of the Valsalva treatment, but now it is only used as an emergency method for relief. Fitcher has shown that there is no evidence to indicate the value of gelatin as a measure to stimulate coagulation in the aneurysmal sac. We do not use the calcium salts either for this purpose. Tufnell's diet is of more recent date. The patient was rested in bed and given a very reduced fare, consisting of 8 ounces of fluid and 10 ounces of solids per diem. This also is very severe. Lowering of blood-pressure, inducing fibrin formation and the benefit of rest, were the claims made for this diet. The rest is of undoubted value, but the supposed increased coagulation of the blood brought about by this method has been disproved by A. E. Taylor on two cases studied some years ago. Clinically the method is more or less discarded. We believe in moderation in this matter. If the case has a fairly high blood-pressure then a light diet is indicated. At the same time we feel that the general nourishment of the patient is to be kept as close to normal as possible. In some of our cases the diet and fluid intake were moderately limited, but in others no change was made. Our impression is that the diet is of minor importance and we can see no advantage in having the patient undernourished.

3. ANTILUETIC TREATMENT. Potassium iodide in moderate doses (gr. xv three times a day) is the drug method of treatment used for many years. The dosage may vary considerably, but the above quantity usually is sufficient for most cases. It undoubtedly has great value, as the severe thoracic pain generally is readily controlled. The ability of potassium iodide to hasten the absorption of luetic inflammatory tissue is to be kept in mind. But, as far as we know the *Spirocheta pallida* is not affected by this drug, hence we cannot hope to stop the inflammatory process in the wall

of the aneurysm by its use alone. As in tertiary syphilis elsewhere, mercury and arsphenamin must be added. Mercury in some form should be given and kept up for the same period as we would demand in syphilis. We have no special preference for the way mercury is to be applied. While under our care in the hospital the daily inunctions were used, but when the patient went home a form taken by mouth was substituted. Gray powder was often the choice.

Arsphenamin (diarsenol) in our hands has been quite safe and of great value. Longcope strongly recommends it in his work. We have given many injections in aneurysms and have never seen any ill results. The doses should always be small and repeated at weekly intervals. We recommend that the patient receives at least 12 injections, each of the first six being 0.2 gm. and the remainder 0.3 gm. We never give a larger dose, as we desire the patient to be free from any straining as would occur in vomiting. The arsphenamin is given while the patient is resting in bed, hence the value of making the primary rest as long as possible. In one case we gave fifteen injections. We have no definite rule, save the general condition of the patient and the Wassermann reaction to know when to discontinue the therapy. This is a very difficult problem to decide in aneurysm or in any form of syphilis. It is our intention to treat all cases actively for at least two or three years if this is feasible. We lay great importance to the frequently repeated small injections of arsphenamin at the onset during the period of rest. This is really all we have to offer, namely, treat aneurysms intensively by antiluetic measures. There is, of course, nothing new in the method, but, taking the disease as a whole, one would be surprised, we believe, to know how few aneurysms ever receive mercury or arsphenamin. From our experience there is no contra-indication to the use of the latter drug. We have given it, with very gratifying results, in a case in which the aneurysm was of enormous size, bulging through the chest wall. The solution given was never more than 100 c.c., and always diluted at least in the proportion of 0.1 gr. for every 25 c.c. of distilled water.

The following is a brief report of the salient points of our cases. From this very small list and the short duration under treatment it would be unwise and further incorrect to be too sanguine as to the ultimate value of the therapy, but there are some points which have been so different from our past experience that we feel justified in continuing this method and in presenting these facts:

We have had seven cases to observe in a period of three years, four of these are unsatisfactory from the point of record in that we have lost track of them since leaving the hospital. They seemingly did not wish to coöperate even while in our care. They were given four injections of arsphenamin (0.2 gm.) each during the month spent in the hospital in addition to the mercurials and iodide, but

at the end of this time they departed against advice. Subjectively they were free from symptoms, and this is probably why we were not able to hold them further. Despite promises to return for observation they have been entirely lost sight of. It would be very unwise to say anything further on this group, except that they took the antiluetic treatment well and improved with one month's rest. Two of these aneurysms had all the physical signs of being large and well advanced.

Of the other three we have more complete records. They are under our observation from time to time.

CASE I.—O. K., aged thirty-six years, molder, primary lesion fifteen years before onset of symptoms, enjoyed excellent health until July, 1916, when he suddenly developed attacks of dyspnea of a paroxysmal type, accompanied by substernal pain. He was sent by his physician to Dr. B. M. Dickinson for a nose and throat examination. This was negative, and he was referred to the medical service of Dr. J. A. Lichty in August, 1916, or six weeks after his first symptoms. The physical examination showed a very apparent pulsation in the first and second interspaces on the right and in the episternal notch, with a distinct lifting of the sternal end of the right clavicle with each pulsation. An expansible character was noted by palpation. There was increased dullness to the right of the sternum above the level of the upper border of the third rib. The heart sounds had the peculiar quality heard in dilated aorta and further showed a systolic bruit. The auscultatory signs were most evident just under the clavicle. Roentgen rays showed an enlargement of the ascending aorta, with a sacular-like bulging where it curved into the arch. The arch was but moderately involved in the dilatation while the descending thoracic aorta appeared normal. By fluoroscopy an expansile pulsation in the aortic bulging was clearly seen. The Wassermann reaction was positive. The heart appeared normal, as did the rest of the systems. There could be no doubt of the diagnosis of aneurysm of the ascending and of the arch of the aorta.

The patient was eager to get well and remained in bed six weeks. He was given a general diet and allowed to go to the toilet. Potassium iodide, gr. xv, three times a day, 5j of ung. hydrargyrum rubbed into the skin daily, and 0.2 gm. arsphenamin once a week for six weeks was the therapeutic procedure while he was in the hospital. He showed no untoward symptoms after the intravenous injections. He had two attacks of dyspnea during the first week in the hospital, but after this he was free from symptoms and confessed to feeling perfectly well. On his discharge, as he was an intelligent fellow, we instructed him to keep up the iodide and the mercury inunctions which he has followed, we believe, faithfully for three years. The dose of the iodide was, however, diminished, as lately he has become somewhat intolerant to its use. He returned

weekly to the hospital for one month after discharge and four doses, 0.3 gm., arsphenamin were given. In January, 1917, he had three more injections of 0.3 gm. arsphenamin. This was the final number. We have now taken him off mercury after a three years'

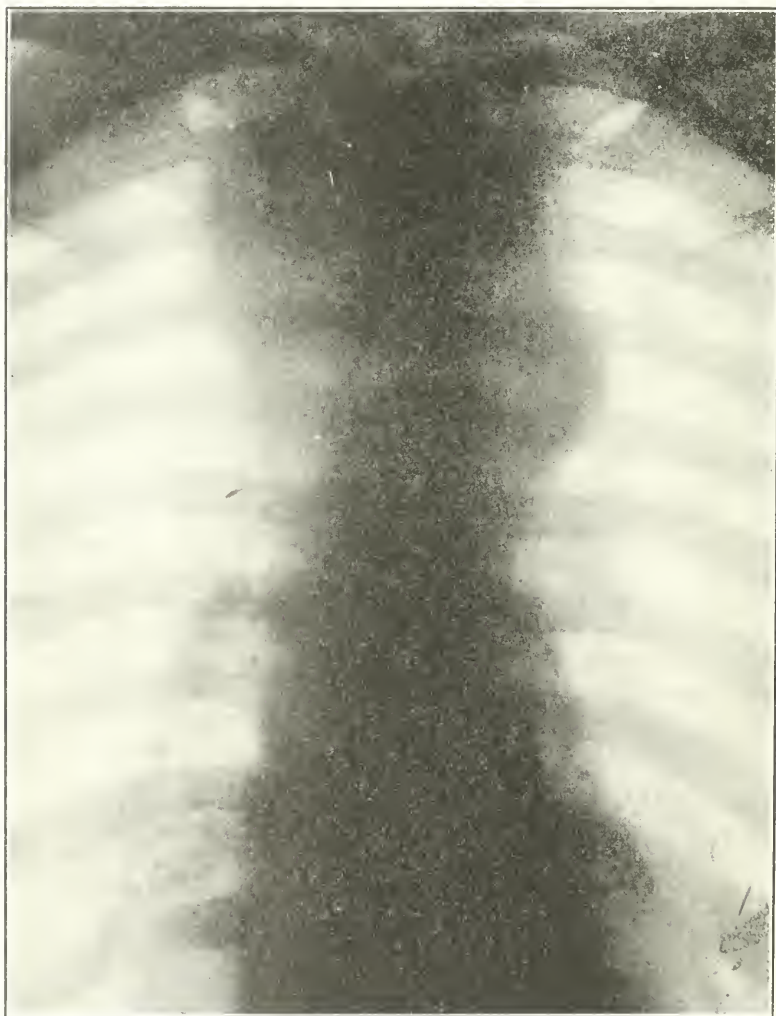


FIG. 1.—Case I. Plate taken shortly after admission to hospital in July, 1916.

course. A rapid review for the past three years has some points of interest: He has been apparently perfectly well and has worked almost every day since leaving the hospital. We cautioned him against working too hard, but to no avail. Before leaving the hospital our intern, with most characteristic teutonic diplomacy,

told him frankly that his case was hopeless and some day he was going to choke to death. This remark we know has never entirely left his mind and accounts for his subsequent, almost foolhardy actions in working. In July, 1917, one year after the onset, he was in apparent perfect health, the Wassermann was negative, but we could get typical physical signs of an aortitis or a dilated aorta,



FIG. 2.—Case I. Plate taken three years after in September, 1919. Note the line of calcium deposit in the wall of the sac.

and the roentgen rays showed almost the same picture as it did the previous year. He was able at this time to pass a fairly close physical examination into a large manufacturing concern, where he made shells for eight months. This work entailed the lifting of 130 pounds (the shell weight) between 100 and 120 times a day, certainly the last thing in the world for a man with an aneurysm to attempt. The reason for this was an economic one: shell-making

was a remunerative job, and he desired to leave as much as possible to his family, firmly believing that the ill-advised remark of the house man might come true any day.

He, however, appeared to be none the worse for this physical test, but was willing to get much lighter work, which he has been doing up to the present. Even the present work, in charge of the repair shop of a garage, gives him very long hours and is relatively hard. Six months ago he fell off a ladder and broke the seventh rib in the anterior axillary line. At that time he noticed very carefully for any sign of pain or discomfort over the aortic area, but none was present. Today he feels perfectly well, looks outwardly in good health, shows signs of slight aortic dilatation, which we would call an aortitis if this were the first examination. His Wassermann is negative. The roentgen rays indicate that he still has his dilated aorta, or aneurysm, with some calcification in the sac wall. There is no expansile pulsation to be palpated, and there is very little evident expansion under the fluoroscope. We do not believe the sac has enlarged.

This type of aneurysm, of course, is the favorable one, and we probably saw it fairly early, although he must have had his aortitis for a considerable time. We trust the sac is filled with organized clot, but we do hope there are no living spirochetes in the wall of the aorta or elsewhere. We are under the impression that if fibrous tissue has replaced all the damage done to the coats of the aorta that this reparative process will, from the point of view of function, carry on for some years.

CASE II.—P. G., aged thirty-five years, laborer, came to the hospital July, 1918, with a pulsating mass protruding in the second right interspace immediately to the right of the sternal border. He complained of some coughing and pain of a sharp, cutting character, usually noticed at night in the chest under the sternum; he could only sleep sitting up in bed or in a chair, could not lie on his side nor could he bend over, and he was forced to stop work on account of the pain produced on using his arms. He is an Italian, and during his stay at the hospital was most difficult to handle. The diagnosis was so evident that we are only mentioning one or two points. The pulsating expansile mass on the right side of the upper chest protruded between the second and third ribs. It was round at the base, having a diameter of 4 cm., the ribs being pushed apart, and it extended outward 2 cm. from the chest wall. The surface had a gentle curve, with a tendency to taper toward the outermost portion. A very marked enlargement of the aorta, by percussion, was easily demonstrated on both sides of the sternum, and the roentgen-ray plate showed the aortic shadow to be as large as the heart. The ascending aorta, arch and part of the descending thoracic aorta was involved. The fluoroscope showed it to be a pulsating expansile mass. Undoubtedly the aneurysm was a very

large one. The Wassermann was positive. The primary lesion was denied. There was a slight regurgitant aortic lesion, but not a great amount of cardiac hypertrophy was present, and the heart's action was regular and of good quality.



FIG. 3.—Case II. Plate taken at the time of admission. (The roentgen-ray plate made fifteen months afterward showed a shadow similar to the above, but unfortunately it was not clear enough to reproduce, and we have been unable to get the patient to return for another.)

We were very unwilling to try arsphenamin, and, in fact, kept him under observation for two weeks before giving the first injection; but we concluded that from the man's point of view it was worth the risk. It was the size of the aneurysm that made us hesitate. He took the arsphenamin perfectly and was given ten 0.2 gm., and four 0.3 gm., in all over a period of fourteen weeks. Potassium iodide, gr. xv, three times a day, and a daily inunction of mercury

were given while in the hospital, a period of sixteen weeks. These last two preparations had been used from the first. After leaving the hospital we gave him gray powder and iodide, as we felt sure he would not apply the ointment. We now know definitely he has not taken any medicine since leaving us. It was practically impossible to get him to stay in bed, and only on account of his interesting lesion did we tolerate his disobedience. After two months the aneurysmal sac protruding from the chest wall showed signs of decreasing in size, and at the end of sixteen weeks it had entirely disappeared, the chest wall anteriorly resuming a normal contour. The second and third ribs had a normal relationship, although we could distinguish on palpation some irregular thickening along the free margins. In the interspace one could readily get the pulsating sac with the tip of the finger. This disappearance of an aneurysm from the surface is known to occur, and it sometimes happens at the expense of growth of the sac elsewhere. We had no indication, however, of this occurring. The patient during the last month seemed to appreciate he was improving, and we were able to get him to rest in bed for a few hours during the day. His symptoms, save for an occasional brassy cough, disappeared, and he left the hospital feeling well and intending to go back to work at once on a light job. His Wassermann reaction at the end of his hospital stay showed a negative fixation with the lipoid, but definite positive with the cholesterolin antigen. The roentgen-ray picture gave a shadow of about the same size as at the onset. He was on a general diet. After leaving the hospital, which he did on account of the inrush of influenza patients, we heard of him only indirectly. It was impossible to get him to report, and only through the kindness of one of the officials of the steel company where he was employed were we able to get in touch with him. After fifteen months he made his first appearance, and he really looked very well. He has been working steadily since leaving the hospital, and his work has not been at all times, by any means, what we would call light or easy. The physical signs are just what they were when he left. The roentgen rays and fluoroscope show that the sac has not changed any in that time. He stopped taking mercury and potassium iodide the day he left the hospital, as we imagined he would. The Wassermann reaction now is strongly positive with both antigens. We gave him some good, sound advice, put him back on mercury and iodide and commenced another series of arsphenamin injection, but after two weeks he again disappeared, and in all probability will not return until he develops more symptoms. Unfortunately, however, we are losing or have lost the good start we made last year in this case. It is too bad that this patient is so refractory, because if one could get some results with an aneurysm of this size under difficulties then we should be able to do a great deal more when conditions are more favorable. This aneurysm is undoubtedly very large, and

when we consider that over a year ago he was not able to sleep except sitting up, could not bend over or lie on his side, and had a very harassing cough, with a good deal of thoracic pain, we must conclude that from the point of general well-being he is clearly improved. This we would hardly expect without treatment after fifteen months in an aneurysm of this size. It is further very unfortunate he did not take the mercury as directed during the past year.

CASE III.—W. R., aged forty-two years, was admitted to Dr. J. A. Lichty's service in August, 1918, suffering from nocturnal dyspnea and severe, almost constant, deep thoracic pain, which at times was cutting in severity. These symptoms appeared in January, 1918, but for the year before that he had been in rather poor health, although not suffering especially from the chest symptoms. A very large aneurysm, involving the greater part of the thoracic aorta, was readily apparent on physical examination. A diffuse throbbing pulsation of the whole upper chest and vessels of the neck, dulness on both sides of the sternum above the cardiac area, particularly on the left side, tracheal tug, systolic murmur over dull area, expansile enlargement almost of the heart size by fluoroscopic examination and roentgen-ray plate, typical of a large thoracic aneurysm, chiefly of the arch and first part of the descending aorta, could be made out. The Wassermann was strongly positive. There was a regurgitant lesion at the aortic valve and some left-sided cardiac enlargement. Compensation appeared to be good. An indefinite primary lesion was present twenty years ago. He remained in bed for the month of August. He unfortunately could not rest for a longer time, as it was practically impossible for him to get away from his business. He was virtually alone for one continuous year without a day off, after his rest in the hospital managing a busy retail hardware store in one of the very active towns of this district, and to make matters worse, the influenza epidemic carried off his head clerk, so that for this patient mental and physical rest, which, is so important, was not only absent, but the opposite state of affairs existed. He was forced to follow this course, knowing the dangers, but as his partner was an officer in France, he felt it to be his duty to conduct the business even to his own detriment. Potassium iodide and mercury have been faithfully followed for fourteen months. He was given six intravenous injections of arsphenamin 0.2 gm. during the first six weeks and two courses of three injections of 0.3 gm. at weekly intervals in October and November, 1918. There was no reaction after any of these injections. The dyspnea had disappeared by the time he left the hospital, but he continued to have some thoracic pain for two months longer, but this was very mild in comparison to what it had been. He has reported about once a month up to the present time. At this date, which is fourteen months after the treatment

began, he is much improved. He occasionally has had slight thoracic pain, but it is a very infrequent occurrence now. There is no dyspnea. He is able to sleep readily, a thing which one year ago was impossible. To use his own words, "He feels 100 per cent. better today than one year ago." The physical signs, however,



FIG. 4.—Case III. Plate taken fourteen months after the beginning of treatment. (The first roentgen ray at the time of admission was broken, but the report on it would indicate a shadow of somewhat the same type as the above.)

really do not show much change. The roentgen-ray shadow is of an alarming size. There is a very definite diminution in the visible thoracic pulsation, but otherwise the signs are about what we described. The Wassermann is negative. He has gained twenty pounds since the treatment began. We intend to give more arsphenamin, and of course continue the mercury and iodide for a

year or more at least. The aneurysm in this patient is also a large one. At the end of fourteen months he is certainly in much better shape, having put on twenty pounds in weight, and now being practically free from symptoms. The diminution in the heaving pulsation over the upper chest, which was most marked one year ago, is very noticeable. This is about the only outstanding change in the physical signs. He is fortunately now situated in such a way that he will be able to take more rest. Here, again, the general improvement after a period of over one year is rather more than one would expect from a case of this type.

DISCUSSION. We frankly admit that our cases are too few in number and the time under treatment too short to allow us to make any dogmatic statement on the prognosis of this disease. The opportunity to study cases of this type for considerable periods is not always available, and therefore one must make the best of what is to be had. It is easy enough to observe a fair number of aneurysms, as the condition is by no means uncommon; but in our experience it has been a very difficult matter to keep in touch with these patients. In order to estimate the ultimate value of a *regime* such as we have suggested, it is necessary to follow a number of cases for several years.

We wish to emphasize, however, the general improvement noticed in three cases of aneurysm, two of them of massive size, after a period varying from fourteen months to three years. We are at present inclined to feel that the absence of symptoms, the ability to do the day's work and the general improvement in health are to be taken as the index of the results of therapy. The changing of the Wassermann reaction at the end of the first year is important, but of much more value is the negative Wassermann at the end of several years. We regard it as being very unwise to stop treatment too early on account of a negative complement-fixation.

The physical signs of a dilated aorta and the lack of any special change in the roentgen-ray picture might at first be considered as proving the failure of therapy. This, however, may not be the case. After an aneurysm has developed it is most likely an impossibility for the normal ever to return, and hence the shadow cast is going to be more or less as before. With early sacculations one might expect considerable alteration in the size after treatment, but we hardly look for any change in aneurysms of the size of our last two cases. The roentgen-ray plate does not indicate whether the inflammatory process in the wall has subsided or not. In fact, there is no way of being sure of this point at the present time. As long as the aortic enlargement does not appear to be increasing in size, and associated with this there is a general improvement in the patient we are not going to worry over the fact that the sac shows no signs of returning to the normal. In Case II there was a visible mass in the chest wall which disappeared, but this may not mean

that the whole sac was any smaller. The development of what does appear to be a fine layer of calcium in the sac of the first case three years after treatment began is of interest from several points of view. In the first place calcification and syphilitic lesions of the aorta do not, as a rule, go together. One sees very few aneurysms at autopsy showing any evidence of calcification in their walls. It would be very interesting to know whether the so-called spontaneously healed aneurysm, which we know occurs, has calcium deposits in its wall, and also whether a positive history of syphilis is present. One is tempted to ask if in our case this deposit bears any relation to or is an index of healing. At the present time, however, we are able to do little more than note its occurrence.

We must admit that we are favorably impressed with the results so far observed, and therefore feel justified in recommending more active antisymphilitic treatment for aortic aneurysm.

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THE SIGNIFICANCE OF YELLOW SPINAL FLUID.

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The occurrence of a yellow spinal fluid is sufficiently rare as to excite interest and sufficiently common to merit a brief consideration of its significance. The true syndrome of Froin¹ consists in (1) a spinal fluid which coagulates at once or upon standing—the consistency of the clot varying, but often so tenacious as to permit one to invert the tube; (2) a yellow coloration or xanthochromia; (3) a marked increase in cells and albumin. Froin² and all others who have studied this condition are agreed that the coloration is due to the presence of blood pigments chiefly bilirubin and the increased coagulability to an increase in fibrin. We shall not attempt to review the causative factors, mechanical and clinical, that bring

¹ *Gaz. des hôp.*, Paris, 1903.

² *Syndrome de Coagulation Massive*, *Gaz. des hôp.*, 1908, p. 1587.

about this departure from the usual pathological findings in spinal fluids but proceed to a consideration of the conditions in which it is encountered.

In a description of 100 cases Sprunt and Walker³ state that the majority of cases showing yellow fluid present the complete syndrome but in 96 cases we have only had it occur in six instances. It appears that the true syndrome of Froin represents the highest development of a process in the spinal fluid of which the yellow coloration without the other essentials represents the earliest stage. Our 6 cases that presented the complete syndrome were 2 meningeal hemorrhages, 2 cases of tuberculous meningitis, and 2 of poliomyelitis.

In 95 cases of cord tumors and other chronic surgical conditions of the spinal cord which Elsberg and Rochefort⁴ studied at the Neurological Institute, New York City, they found yellow fluid in 14 cases and spontaneous coagulation in 7 cases—a rather high proportion which would lead me to believe that disease of this kind tends to produce the conditions necessary for the development of the complete syndrome of Froin as stated by Mestrezat⁵ to wit: (1) the existence of a closed cavity shut off from the general circulation in which the elements derived from blood accumulate (by transudation or hemorrhage); (2) an alteration (infectious or toxic) of the vessels of the cavity bringing about a transudation or a number of minute hemorrhages. In Dr. Elsberg's series of cases in which yellow fluid occurred, there were ten extramedullary tumors, two gummas, one varicose vein of the cord, and one neuritis of the cauda equina.

Our series of cases, 96 in all, represent the number of instances in which these cases have occurred in nine years of work of the Meningitis Division of the Health Department. There were 5801 fluids so that the percentage of cases in which yellow fluid occurred was about 1.6 per cent. Of these 96 cases, 60 have been tabulated and accompany this paper in the form of a table which is appended. Thirty-six cases were omitted from tabulation because the diagnosis was never confirmed definitely or there was lack of sufficient data. The chief interest of our series of cases lies in the fact that we see almost exclusively acute or subacute types of disease—which probably accounts for the small number of cases in which the syndrome of Froin occurred in all its manifestations. Our cases were as follows: tuberculous meningitis 40, poliomyelitis 13, cerebral hemorrhage 3, meningeal hemorrhage 1, cord tumor 1, pachymeningitis 1, cerebrospinal meningitis 1.

Yellow fluids occurred in many cases of recovering epidemic meningitis but were omitted from consideration in this paper

³ Significance of Xanthochromia of the Cerebrospinal Fluid, Bull. Johns Hopkins Hosp., 1907, xxviii, 80.

⁴ Xanthochromia and Other Changes in the Cerebrospinal Fluid, Jour. Am. Med. Assn., vol. lxviii.

⁵ Le Liquide Céphalorachidien, Paris, 1912.

TABLE OF YELLOW FLUIDS.

No.	Amount, c.c.	Coagu- lation.	Albumin.	Globulin.	Fehling's.	Cells, per cent.	Diagnosis.
1	60	0	++I solid	++ solid	+1	+ 95 (polys.)	Tb. meningitis.
2	15	+++	+++++	+++++	+1	+95 (monos.)	Poliomyelitis.
3	15	0	+++++	+++++	+	+95 (monos.)	Poliomyelitis.
4	10	0	+++++	+++++	++	+95 (monos.)	Tb. meningitis.
5	5	0	+++	+++++	0	+90 (monos.)	Tb. meningitis.
6	8	0	+++	+++	N.d.	None (?)	Poliomyelitis.
7	3	0	++	+++	N.d.	+	Tb. meningitis.
8	20	0	+++	+++	N.d.	+90 (monos.)	Tb. meningitis.
9	40	0	+	+	N.d.	Red blood cells	Meningeal hemorrh.
10	8	0	+++	+++	N.d.	+95 (monos.)	Tb. meningitis.
11	3	0	+++++	+++++	N.d.	+85 (monos.)	Tb. meningitis.
12	8	0	+++	+++++	+	+60 (monos.)	Poliomyelitis.
13	40	0	+++++	+++++	0	+50 (monos.)	Tb. meningitis.
14	70	0	+++	+	N.d.	90 (monos.)	Tb. meningitis.
15	10	0	++	N.d.	N.d.	Few cells	Paehymeningitis.
16	5	0	++	+++	N.d.	++	Poliomyelitis.
17	5	0	+++++	+++++	+1	+90 (monos.)	Tb. meningitis.
18	10	+	+++++	+++++	+1	+98 (monos.)	Tb. meningitis.
19	40	0	++++I	+++++	+	+95 (monos.)	Tb. meningitis.
20	30	0	+++++	+++++	+1	+90 (monos.)	Tb. meningitis.
21	20	0	+++++	+++++	+	+90 (monos.)	Tb. meningitis.
22	20	0	+++++	+++++	++1	+90 (monos.)	Tb. meningitis.
23	30	0	+++++	+++++	++1	+80 (monos.)	Tb. meningitis.
24	25	0	+++++	+++++	++1	+95 (monos.)	Poliomyelitis.
25	15	0	+++++	+++++	+1	+70 (polys.)	Tb. meningitis.
26	10	0	+++++	+++++	++	+90 (monos.)	Tb. meningitis.
27	25	0	+++++	+++++	+	+90 (monos.)	Tb. meningitis.
28	35	0	+++++	+++++	+1	+90 (monos.)	Tb. meningitis.
29	5	0	+++++	+++++	++1	+90 (monos.)	Tb. meningitis.
30	5	+	N.d.	+++++	+	Few	Meningeal hemorrh.
31	2	0	+++++	+++++	+1	+	Tb. meningitis.
32	5	0	+++++	+++	+++	Slight + 90 (monos.)	Cerebral hemorrhage.
33	30	0	+	+	+++	+	E. C. S. W.
34	35	0	+++++	+++++	+1	+90 (monos.)	Tb. meningitis.
35	20	++	+++++	+++++	++	+70 (monos.)	Meningeal hemor.
36	20	0	+++++	+++++	+	+mod. 90 (mon.)	Tb. meningitis.
37	20	0	+++++	+++++	+	+80 (monos.)	Tb. meningitis.
38	3	0	+++++	+++++	N.d.	N.d.	Poliomyelitis.
39	20	0	+++	+++I	+++	+60 (monos.)	Poliomyelitis.
40	10	0	+++++	+++++	+1	+95 (monos.)	Tb. meningitis.
41	20	0	+++++	+++++	0	+98 (monos.)	Tb. meningitis.
42	5	0	+++++	+++++	+	+89 (monos.)	Tb. meningitis.
43 ⁶	30	0	+++++	+++++	+++	Moderate + monos.	Poliomyelitis.
44 ⁷	25	0	+++++	+++++	+++	+	Poliomyelitis.
45 ⁸	40	0	+++++	+++++	+	+90 (monos.)	Tb. meningitis.
46	30	0	+++++	+++++	+	+90 (monos.)	Tb. meningitis.
47	2	0	+++++	N.d.	N.d.	+	Tb. meningitis.
48	3	0	+++++	+++	+1	+90 (monos.)	Tb. meningitis.
49	10	0	+++++	+++	+	+99 (monos.)	Tb. meningitis.
50	20	0	+++++	+++I	+	+95 (monos.)	Tb. meningitis.
51	40	0	+++++	+++	+++	+90 (monos.)	Poliomyelitis.
52	20	0	+++	+++I	+	+mod. 95	Tb. meningitis.
53	15	0	+++	+++	+++	N.d.	Cerebral hemorrhage.
54	10	0	+++	+++	+++	+90 (monos.)	Tb. meningitis.
55	30	0	+++I	+++I	+1	+50 (monos.)	Poliomyelitis.
56	60	0	+++	+++	+1	+99 (monos.)	Tb. meningitis.
57	15	0	+++++	+++	+	+95 (monos.)	Tb. meningitis.
58	15	0	+++++	+++	+++	+75 (monos.)	Poliomyelitis.
59	30	0	+++	+++	+++	+90 (monos.)	Tb. meningitis.
60	30	0	+++	+++	+	+99 (monos.)	Tb. meningitis.

⁶ Fluid No. 13, gold chloride curve, 1111, 232100.⁷ Fluid No. 44, gold chloride curve, 111, 22332210.⁸ Fluid No. 45, gold chloride curve, 111, 2322100.

N.d., not done.

Summary: Tuberculous meningitis	40
Poliomyelitis	13
Cerebral hemorrhage	3
Epidemic meningitis	1
Pachymeningitis	1
Syringomyelia	1
Meningeal hemorrhage	1

Total 60

because the condition did not occur spontaneously but after the administration of serum, which, however, we do not consider the cause of the xanthochromia.

Mestrezat⁹ and many of the French writers have pointed out that the occurrence of a yellow fluid is not uncommon in tuberculous meningitis, yet it forms a very striking fact that it occurs in over 66 $\frac{2}{3}$ per cent. of our cases. Neal and DuBois¹⁰ have already pointed out that yellow fluids occur too in poliomyelitis.

It had long been my clinical observation which is confirmed by these figures that given a patient with meningeal symptoms who on lumbar puncture shows yellow spinal fluid one should be inclined to a diagnosis of tuberculous meningitis or poliomyelitis—this evidence, of course, being by no means conclusive but merely a factor to be considered in the other points of diagnosis which further study of the spinal fluid usually decides.

The spinal fluid withdrawn in these cases has varied in amount from 3 c.c. to 50 c.c. The color has ranged from the faintest of yellow tints to the deepest canary. The albumin and globulin have been markedly increased in the majority of the cases. The sugar reactions as shown by the reduction of Fehling's solution has varied with the underlying etiological infection. In three instances colloidal gold curves were performed and these are included in the table.

RÉSUMÉ. (1) Yellow spinal fluid occurs in a wide range of diseases of the spinal cord and meninges; (2) the complete syndrome of Froin is comparatively rare in its occurrence; (3) in acute or subacute conditions the presence of yellow fluid strongly suggests the probable diagnosis of tuberculous meningitis or poliomyelitis.

**THE OCCURRENCE OF GLYCOSURIA IN MUSHROOM-POISONING,
WITH THE REPORT OF FIVE CASES IN WHICH A MILD
NEPHRITIS AND A RENAL GLYCOSURIA WERE THE
PERSISTENT AND PREDOMINATING FEATURES.**

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ALTHOUGH the history of mushroom-poisoning reaches back to the times of Babylonia and ancient Rome, most of the reports, even the more recent, give but little clinical details and no accurate account of postmortem findings. In reviewing the literature one is also impressed by the few reports of cases that have ended in recovery. Although recent investigators, as Clark, Marshal and

⁹ Same.

¹⁰ The Diagnosis of Poliomyelitis, AM. JOUR. MED. SC., September, 1916.

Rowntree,¹ have emphasized the urinary findings and the blood chemistry in cases of mushroom-poisoning,² I can find no reference to the occurrence of glycosuria in such cases. In a personal communication from Dr. Carl Th. Mörner of Upsala, who recently published an exhaustive treatise on poisonous mushrooms (*Om de Högre Svamparna*, Upsala, 1919), he writes that he has never met with a case of glycosuria following mushroom-poisoning, nor has he read any account of it in his review of the literature.

It is not necessary in this place to review the history of mushroom-poisoning. The subject has recently been reviewed by Mörner in *Upsala Lakareforenings Forhandlingar*, January 20, 1919, pp. 1 to 57, also in the work mentioned above. It may be of interest to note that one of the earliest clinical reports in the literature is by Cheney,³ although no postmortem findings are given. Caryon,⁴ in 1873, reported the clinical course of a fatal case, and Adolph Kessler,⁵ in 1880, reported the urinary and clinical findings of acute nephritis in a fatal case, as was also proved at autopsy. Michel⁶ reported some cases in 1876, Ore,⁷ in 1877 and Plowright,⁸ Palmer,⁹ and McGlenn¹⁰ in 1879. Schröter¹¹ and Trask¹² also reported cases in 1883. Studer, Sahli and Schärer,¹³ in 1884, collected all previous cases of poisoning that had autopsies performed and also reported several new cases. The pathological findings generally encountered were ecchymoses and hemorrhages in serous membranes and parenchymatous organs, together with profound fatty degeneration in liver and kidney. The heart may be found in a state of dilatation. The lungs are congested and bronchopneumonia of the hemorrhagic type is frequently encountered.

Although acute nephritis has long been recognized as a manifestation of mushroom-poisoning, it is only recently that a careful study of the urine and blood was undertaken by Clark, Marshall and Rowntree.¹⁴ In none of their cases was there any evidence of any nitrogen retention in the blood. The phenolsulphonophthalein output was generally quite low, 33 per cent. in one of the cases that recovered.

In the cases forming the basis of the present paper, glycosuria was present in addition to the evidences of a mild nephritis.

¹ Jour. Am. Med. Assn., April 10, 1915, pp. 1230-1232.

² By *Amanita Phalloides*.

³ Cases of Mushroom-poisoning, *Pacific Med. and Surg. Jour.*, 1871-2, v, 119-121.

⁴ *Gaz. des hôp.*, 1873, p. 1146.

⁵ Fatal Poisoning by Mushrooms, *AM. JOUR. MED. SC.*, October, 1880, pp. 393-399.

⁶ *Gaz. hebdom. de méd.*, 1876, p. 657.

⁷ *Compt. rend. Soc. de biol.*, lxxxiii, 837.

⁸ *Lancet*, December, 1879, p. 941.

⁹ Toadstool-poisoning, *Boston Med. and Surg. Jour.*, ci, 301-304.

¹⁰ Six Cases of Toadstool-poisoning, *Med. Herald*, Louisville, 1879-1880, i, 255.

¹¹ Breslauer Aertzl. Ztschr., 1883, p. 149.

¹² Cases of Mushroom-poisoning, *AM. JOUR. MED. SC.*, 1883, lxxxv, 358-365.

¹³ Beiträge zur Kenntniss der Schwammvergift., *Mitteil. der Naturf. Gesellsch.*, Bern, 1884, p. 85.

¹⁴ Mushroom-poisoning, *Jour. Am. Med. Assn.*, April 10, 1915, pp. 1230-1232.

The five cases occurred in one family. The father was aged forty-nine years; the mother, forty-eight; a daughter, twenty-one; a son, sixteen; and a boy, aged five. The mushrooms, about a pound by weight, were picked in the forenoon of August 28. They were boiled and prepared with milk and butter. It was said that the number of mushrooms consumed by each member of the family was in proportion to age, for the father ate most and the mother and children lesser amounts. About three hours after the ingestion of the mushrooms the father complained of nausea and of pain in the epigastrium. Soon afterward all the others had a similar experience. About two o'clock that morning they all vomited and complained of headache and dizziness. Their vision was blurred and the sensorium somewhat confused. The vomiting persisted all night, each one having vomited eight to ten times. Toward morning they felt a little better and that day they all pursued their daily occupations. For three days they all felt fairly well, although each gives a history of having felt weak, being nauseated and suffering from headache. Their appetite was poor and they ate but little, but took no particular care with their diet, having eaten anything they desired. Gradually their condition became worse and on the fourth day after the ingestion of the mushrooms their headache became intense and they complained of an unpleasant taste in the mouth and marked thirst. They all again commenced to vomit and were markedly prostrated. The father, who seemed most affected at this time, was advised to enter the hospital. He was admitted to the Waterbury Hospital, in the service of Dr. Engelke, on the fifth day after the ingestion of the mushrooms.

The physical examination revealed a well-nourished male, aged about forty years, five feet nine inches tall, and weighing 160 pounds. He was rather pale and the sclerae were slightly jaundiced. The heart and lungs were negative. There was no edema of the extremities and the reflexes were normal. The temperature at the time of admission was 98.4° F.; pulse 80, respirations 20. The blood-pressure was: systolic 128 and diastolic 80. The blood examination showed the hemoglobin to be 85 per cent.; red blood cells, 4,100,000; white blood cells, 8100; polymuclears, 74; lymphocytes, 22; mononuclears and transitionals, 3; eosinophiles, 1. The alveolar air was 35 per cent., determined by the Marriott method.

The urine was cloudy; yellow; 1024; acid; heavy cloud of albumin, 0.75 per cent.; sugar; marked reduction of the Benedict-Fehling reagent (quantitative determination, 2.5 per cent.). The microscopic examination showed amorphous urates and numerous finely and coarsely granular casts, also an occasional white blood cell. There was also a moderate trace of acetone and a faint trace of diacetic acid. There was no increase of indican.

The secretion of urine during the next twenty-four hours was 1700 c.c. The specific gravity was 1022; acid; slight cloud of

albumin, 0.25 per cent.; total, 4.25 gm.; sugar, 2.5 per cent.; total, 38.25 gm.; urea, 0.008 gm. to 1 c.c., total, 13.6 gm. The microscopic examination showed numerous granular and occasional hyaline casts also an occasional white blood cell. There was a marked reaction for acetone and a heavy trace of diacetic acid. The indican reaction was normal.

KIDNEY FUNCTION, ETC., OF C. S. (CASE STUDIED IN HOSPITAL).

Date.	Urine.						CO ₂ alveolar air.	Blood.					
	Albumin.	Sugar.	Casts.		Acetone.	Diacetic.		Urea nitrogen.	Creatinin.	Uric acid.	Sugar.	Phenolsulph. test, per cent.	
			Hyaline.	Granular.									
Sept.	1	0.5	2.5	occas.	num.	++	+	30	40	1.6	1.0	90	15
	3	0.5	2.5	"	"	+++	++	25					
	5	0.25	2.25	"	"	++	+	35					
	7	0.25	2.25	"	"	+	0	35	32	1.4	0.8	80	20
	9	0.12	1.0	"	"	0	0	40					
	11	0.1	1.25	few	mod.	0	0	45					
	13	v. f. t.	0.75	"	"	0	0	45					
	15	v. f. t.	0.25	"	few	0	0	45	25	0.8	1.0	70	30
	17	v. f. t.	0.24	"	"	0	0	45					
	19	v. f. t.	0.12	"	"	0	0	45					
Oct.	21	0	0.12	"	0	0	0	15	22	0.4	0.8	65	35
	28	0	0	"	0	0	0	45					60
	5	0	0	0	0	0	0	15	16	0.4	1.2	70	65
	19	0	0	0	0	0	0	45	14	0.5	...	80	80

The subsequent urinary findings, together with the blood chemistry and other laboratory examinations, are set forth in the accompanying table. As will be seen from this tabulation the glycosuria was more prominent and more persistent than the albuminuria. There was a very slight retention of urea nitrogen, and creatinin in the first two determinations. The sugar content of the blood was decidedly normal throughout. The phenolsulphonephthalein output was very low at first and remained low even after the urine showed no albumin and no casts.

On the fifth day after admission the patient was given 100 gm. of glucose and the urine was examined quantitatively every hour. The sugar output varied from 2.5 per cent. to 2.25 per cent. There seemed to have been no increase in the sugar output in the urine following the ingestion of the glucose; since the day before similar quantitative determinations made every hour showed a similar slight variation. Seven days later these tests were repeated, with the same results.

As regards the patient's symptomatology for the first forty-eight hours after admission to the hospital, he complained of considerable headache, nausea and marked weakness. He was given a saline cathartic and the rest of the treatment was that of a mild nephritis.

Potassium acetate and potassium citrate, $\bar{a}\bar{a}$ gr. x, were given every four hours. His diet consisted of milk, cereals and cooked vegetables. Spices, broths and meat extracts were prohibited. The glycosuria was considered a secondary manifestation and no special attempt was made to deny the patient carbohydrates. As can be seen from the accompanying chart the urine has returned to normal at the end of the fourth week, although the subjective symptoms disappeared shortly after admission to the hospital.

The symptoms, urinary findings and entire course of the other four patients that partook of the mushrooms were exactly similar to those of the father, as already described. The urinary picture of one was almost exactly the same as of any of the others. There was the same amount of albumin and the same predominance of granular casts and scarcity of hyalin. The mother's urine had 2.5 per cent. sugar; the daughter, 2.75 per cent.; the son, 2.5 per cent.; the boy, 2.25 per cent. Even the duration was exactly the same, four weeks having elapsed before the urine entirely cleared up.

Among the mushrooms that were left uncooked there was one specimen that was identified by Professor Lafayette B. Mendel, of Yale, as an *Amanita muscaria*. The rest were *Agaricus campestris*. Two other people ate everything at that meal except the mushrooms, and they had no untoward symptoms whatsoever.

It is well known that in addition to phloridzin there are numerous chemical substances that may produce glycosuria. To enumerate them briefly one may mention the caffein group,¹⁵ curare,¹⁶ strychnin,¹⁷ carbon monoxide poisoning,¹⁸ amyl nitrite,¹⁹ chloral,²⁰ sodium chloride,²¹ phosphorus-poisoning²² and several others. Recently, Salant and Wise²³ produced glycosuria experimentally by means of the zinc salts.

The phloridzin diabetes has been the one most thoroughly investigated. Since von Mehring²⁴ first reported upon it in 1886 numerous investigators have repeated and amplified upon his findings. It was not only demonstrated that phloridzin acts upon the kidney substance by lowering its permeability point to sugar, but it was also shown what part of the kidney is acted upon. In con-

¹⁵ Jacobi, C.: Ueber künstlichen Nierendiabetes, Arch. f. exp. Path. u. Pharm., Leipzig, 1894-95, xxxv, 213-221.

¹⁶ Jones H. V.: Zur Erklärung des Curare Diabetes, Arch. f. Phys., Leipzig, 1891, pp. 476-479.

¹⁷ Gerloff, C.: Beiträge zum Strychnin Diabetes, Kiel, 1888, 80.

¹⁸ Garafaola, A.: Recerche speriment. sulla glicos. per assido de Carbonio e per gas illuminante, Bull. d. r. Acad. méd. di Roma, 1891, No. 2, xviii, pp. 191-221.

¹⁹ Galeotti, G.: Ueber cinige neuere Unters. über exp. Glicos. u. Aceton, Centralbl. f. allg. Path. u. path. Anat., Jena, 1892, iii, 289-294.

²⁰ Simon, C. E.: Clinical Pathology, Philadelphia, Lea & Febiger, 1911, p. 358.

²¹ McDanell, L., and Underhill, F. P.: Salt Glycosuria, Jour. Biol. Chem., March, 1917, xxix, 273.

²² Laub, M.: Wiener med. Wehnschr., January 13, 1898.

²³ Production of Glicos by Zinc Salts, Jour. Biol. Chem., May, 1918, xxxiv, 447.

²⁴ Ueber exp. Diabetes, Verh. des Cong. f. inn. Med. Wiesb., 1886, v, 185-189.

nection with his studies of experimental diabetes, von Mehring shows that in phloridzin diabetes the blood shows no hyperglycemia. Clinically, also, renal diabetes is characterized by no increase in the blood sugar. When, in 1896, Klemperer²⁵ reported a case which he called "renal diabetes," he stipulated that in order for such a diagnosis to be made the following postulates must be fulfilled:

1. The glycosuria must be independent of the amount of carbohydrates ingested.
2. There must be no increase of sugar in the blood.
3. The development of a nephritis decreases the glycosuria.

Subsequent investigations of these cases of "renal diabetes" showed that the second postulate is absolutely correct, but the first and third are not necessarily to be fulfilled. The characteristics of renal glycosuria have been succinctly stated by Allen²⁶ as "Glycosuria, with normal glycemia, relatively independent of diet."

The literature on this subject has recently been reviewed by Bailey,²⁷ and Lewis and Mosenthal²⁸ have given an excellent review of the cases so far reported.

It will, hence, be seen that the cases of glycosuria in mushroom-poisoning described above will very likely fall into the group of renal glycosuria.

PULMONARY COMPLICATIONS OF PARATYPHOID FEVER, WITH A REPORT OF FOUR CASES.

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DURING the past four years we have had the opportunity of studying 6 cases of paratyphoid fever, and of these 4 have been associated with severe pulmonary disturbances during the course of the paratyphoid infection. In the army during this same period much attention has been paid to the prevention of the disease in the way of sanitation and by protecting the individual by a prophylactic immunization in using the triple vaccines, but the detection of chronic carriers has not had the emphasis put upon it that it deserves. It is in the civilian population that these periodic outbreaks of the paracolonic infections, probably due to chronic carriers, will occur from time to time.

²⁵ *Verein. f. inn. Med.*, Berlin, May 18, 1896.

²⁶ *Glycosuria and Diabetes*, Boston, 1913, p. 511.

²⁷ *Renal Diabetes*, *Am. Jour. Med. Sc.*, No. 2, clvii, 221-236.

²⁸ *Johns Hopkins Hosp. Bull.*, 1916, xxvii, 133.

In the late winter months of 1915 our attention was called to the association of pulmonary lesions in paratyphoid fever in a young adult male admitted to the wards of Dr. Joseph Sailer, with frank lobar pneumonia. His condition progressed favorably and his lungs entirely cleared, but the fever still persisted. The pneumonia was of short duration, and we were much puzzled by the continuance of the fever with an otherwise complete symptomatic recovery. The man was not septic and the blood culture was negative at this time. In the course of a few days the patient had a large hemorrhage from the bowels, followed by several small hemorrhages. At this time the Widal reactions for *Bacillus typhosus* and *Bacillus paratyphosus A* were negative, but it gave a strong, positive agglutination for *Bacillus paratyphosus B*. The blood culture again was negative. The second series of agglutination tests confirmed the first, and subsequently the *Bacillus paratyphosus B* was isolated from the stools. The patient made an uneventful recovery. This case stimulated our interest in the subject, and since that time we have had the opportunity of observing 3 additional cases showing pneumonic complications occurring among the 5 cases observed by us since that time.

It was not until Achard and Bensaude,¹ in 1896, isolated the bacillus and reported 2 cases, which they called *fièvre paratyphoïdique*, that the disease was recognized as a distinct entity. Widal and Nötecourt, in 1897, were successful in isolating the same bacillus from a post-typhoidal abscess. Gwyn,² in 1898, was the first to isolate and culture the *Bacillus paratyphosus* from the blood during life. From this time until 1902 we find but 24 cases reported in the literature; these do not include the Saarbrücken epidemic of 38 cases, as they were not bacteriologically certain to be paratyphoid fever. It is of interest to note that at this time the reports included cases from Germany, France, England, the United States and the Philippines, showing the wide geographic distribution of the infection. This same year Longscope³ reported 2 cases, with autopsy records of 1, in which he stated the presence of extreme congestion and moderate edema of the lungs. Herpes labialis was present in both his cases. Coleman⁴ also reported that herpes occurred in 50 per cent. of the cases and stated that a mild bronchitis was one of the initial symptoms. Bronchopneumonia was also mentioned as a complication at that time. He quotes an epidemic in Middlesboro, in 1888, caused by eating poorly cooked pork in which pleuropneumonia was quite frequent. Autopsy confirmed the clinical manifestations. Coleman was of the opinion that this epidemic was caused by one of the paracolon group, probably the *Bacillus psittacosis*.

¹ Bull. et mém. Soc. méd. de hôp., Paris, 1896, xiii, 820.

² Johns Hopkins Hosp. Bull., 1898.

³ AM. JOUR. MED. SC., 1902.

⁴ Am. Med., 1902, iv, 498, 578, 622.

In 1909 Proescher and Roddy⁵ report an epidemic of 48 cases in Pittsburgh in which cough and bronchitis occurred in 12, or 25 per cent. Acute catarrhal laryngitis was an early symptom. Pneumonia occurred in only one instance, and this patient had been home, sick in bed, for three weeks prior to admission. The pneumonia was lobar in type and involved both lungs. Hoskins,⁶ in the epidemic at Wayne's Cave, Virginia, in the spring of 1909, reports a bronchitis of a persistent character, lasting for several days after the temperature had become normal, in 23 of the 35 cases. This epidemic was due to *Bacillus paratyphosus* B, while the Pittsburgh epidemic was due to *Bacillus paratyphosus* A. In our series of 4 cases 3 were due to the type B infection. In this country the outbreaks have been followed chiefly from a bacteriological standpoint and very few of the observers have mentioned the clinical manifestations.

In the spring and summer of 1916 we had the privilege of studying 2 cases of paratyphoid fever, both of the B. type and both associated with frank evidences of a bronchopneumonia—one of a lobar distribution while the other involved both lungs.

Case No. G, 3914. G. N., adult, male, aged twenty-five years, Italian, laborer, was admitted February 14, 1916, complaining that he had "caught cold," with pain in the lower part of the abdomen, headache and general weakness. Upon examination the patient looked very ill, had a temperature of 103° F., pulse 84 and respirations 30. The spleen was palpable and rose spots were present. Over the right lower lobe the percussion note was dull, the breath sounds exaggerated and many rales were present. Vocal resonance was also increased. Five days after admission his temperature became normal, to be followed the next day by spitting up a mouthful of blood, sharp elevation of temperature to 102.3° F., and an increase in the respiratory rate. The physical findings at the right base had become intensified and were those of a frank bronchopneumonia of the lobar type. At this time the blood culture was positive for *Bacillus paratyphosus* B. It was again positive for the same organism three days later. The patient recovered and, in all, the fever lasted nine days. The sputum was not cultured for the *Bacillus paratyphosus*.

This is the type of case which could easily be taken for any of the acute respiratory infections, and might easily become the source of an epidemic of paratyphoid fever.

Case No. 3. G. M., admitted August 22, 1916, complained of dizziness, anorexia, being unable to work and headache which had become worse three days prior to admission. On examination his teeth were in bad condition, tongue dry and coated. A respiratory grunt was noted, but the lungs were found to be clear except for a

⁵ Jour. Am. Med. Assn., February 6, 1909, p. 170.

⁶ *Ibid.*, 1910, liv, 930.

few scattered rales below the angle of the scapula of the left side. The heart was normal. Splenic area of dullness was increased, but the spleen was not palpable. Rose spots were absent at this time. Temperature on admission was 103° F., pulse 82, respirations 40. Widal reaction for *Bacillus typhosus* was negative. The general condition remained the same for six days, when marked evidences of a very severe bilateral bronchopneumonia made their appearance. At this time the blood culture was positive for *Bacillus paratyphosus* B. His temperature continued for sixty-two days, but he finally made a complete recovery. During his illness his ears, which upon admission had shown a bilateral chronic purulent otitis media, were irrigated frequently each day, to keep them free from pus as nearly as possible. At this time, sixty-two days after admission and sixty-five days after the beginning of his illness, we were able to isolate the *Bacillus paratyphosus* B from the pus of the otitis media and also from around the teeth.

The finding of the bacillus in the discharge from an otitis media and from around the teeth indicates another means by which a patient may become a chronic carrier and through which the spread of the disease may take place.

During the war, epidemics of paratyphoid fever were rather frequent and were of sufficient magnitude to cause armies to be immunized against the infection by vaccination, however, much valuable data from a pulmonary standpoint had been collected in the interim. In October, 1915, Robinson⁷ reported an epidemic of 89 cases in which the *Bacillus paratyphosus* had been isolated from the blood, feces or urine in 47 cases. The remaining 42 cases were clinically paratyphoid fever. Out of the 47 cases in which the bacteriological examination left no doubt as to the correctness of the diagnosis 23 gave a history of an initial chill; cough was present or had been in 26 of the 47 cases. The cough was nearly always loose in character and usually subsided rapidly. There was a history of doubtful hemoptysis in 2 cases. Definite signs of a bronchitis were recorded in 4 cases. Herpes labialis was recorded in only two case histories. Wiltshire⁸ reports an epidemic of 98 cases in the British Expeditionary Forces. A positive bacteriological examination was obtained in 50 cases; 9 were due to *Bacillus paratyphosus* A and 41 were due to *Bacillus paratyphosus* B. In this epidemic pulmonary complications were present in 67.3 per cent. of the cases. Of these 33 had a slight generalized bronchitis, which occurred about the fourth day of the disease, while 19 cases had a frank bronchopneumonia and 5 were lobar in type. Of these 5 lobar pneumonias, 4 had acute pleurisies overlying the areas of consolidation. The fifth lobar patient developed an empyema and

⁷ Lancet, October 16, 1915.

⁸ Clinical Observations of Ninety-eight Cases of Paratyphoid Fever, Practitioner 1915.

died. No autopsy was performed and the culture from the empyema remained sterile, although the pus had the odor of a *Bacillus coli* infection. The sputum in these cases showed the pneumococcus, *Micrococcus catarrhalis*, streptococcus and influenza bacillus. As far as could be determined, the sputum was not cultured for the bacillus paratyphosus. In this series the men were only protected against the *Bacillus typhosus* by inoculation. Wiltshire was of the opinion that many of these cases could easily be mistaken for influenza or gastro-enteritis, as the attacks may be of short duration, in this way giving many opportunities for the carriers, as well as those actually sick with the disease, to spread the infection. Stol-kind⁹ describes a distinct respiratory form of paratyphoid fever in which the symptoms resemble those of influenza. He reports a case in Moscow, in 1916, in which the patient was suddenly attacked with a coryza, cough, headache, moderate fever and lassitude. The spleen was enlarged and rose spots were present. Bacteriologically the *Bacillus paratyphosus* was found. The fever lasted fourteen days. Beteceaw reports a similar case also occurring in Moscow. Baer observed an epidemic of paratyphoid B in 52 soldiers, all of whom had conjunctivitis and pharyngitis; many also had bronchitis. Grattan and Wood, and also Sufford, report cases of paratyphoid A occurring in British soldiers in India in which the attack might easily be mistaken for influenza. In half the cases there were sore-throat and bronchitis. Wilucki also reports an epidemic of 33 cases of paratyphoid bacillus in 7 of which the illness began with acute respiratory manifestations. Wilcox¹⁰ describes a respiratory form of the disease and mentions that pneumonia of the bronchopneumonic type is not uncommon in the severe cases.

In France the army surgeons called attention to the same clinical phenomenon at this time. E. Joltrain et Petit Jean,¹¹ from the First Army, reported 19 cases of pleurisy occurring in 310 cases of paratyphoid fever. Of these 2 were due to empyema; 2 were dry pleurisies and the remaining 15 were serofibrinous. Of the 19 cases 18 were due to *Bacillus paratyphosus* B and 1 to *Bacillus paratyphosus* A. Also in our cases the *Bacillus paratyphosus* B type of infection seemed to be the one which gave us the greater number of pulmonary complications. In all cases the effusions were small, and cytologically they resembled a tuberculous pleurisy. The pleurisy was often the initial symptom, the paratyphoid infection being latent. This was also true in one of our cases of lobar pneumonia in which the paratyphoid had not been suspected until after the subsidence of the pneumonia. In this same connection Florenzano¹² believes that paratyphoid fever is always a septicemia, but

⁹ Respiratory Form of Paratyphoid Fever, *Lancet*, January 15, 1916, p. 136.

¹⁰ *Lancet*, February 26, 1916.

¹¹ Pleurisy in Paratyphoid Fever, *Arch. de méd. et pharmacie Militaires*, 1916.

¹² *Gazzetta degli ospedali e delle cliniche*, Milan, December 7, 1916, No. 98, xxxvii, 1537.

the main focus of infection may be in various organs in different cases. In a case described in detail the localization was in the pleura, and the symptoms of this had preceded the paratyphoid septicemia. The disease ran a course through a period of three months, the toxic and infectious symptoms recurring in three different attacks. In this series of cases pleurisy occurred in 6 per cent., while in typhoid fever the complication is noted in from 2 to 4 per cent.

From the pathological viewpoint, Saquépée, Burnet and Weisenbach,¹³ from the Fourth Army, report the macroscopic findings of 9 autopsies of cases in which the *Bacillus paratyphoid A* had been found before death. In all cases the pulmonary lesions in the form of intense congestion and edema were constant. There were also 2 cases of bronchopneumonia, 1 of a lobar type (left lower) and the other of a lobular type associated with a large empyema. Merklen and Trotain¹⁴ report the autopsy findings in 15 deaths which occurred in 446 cases. Of these 10 were due to *Bacillus paratyphosus B* and 5 to *Bacillus paratyphosus A*. Pulmonary complications were the immediate cause of death in 6 cases. Again at this time Dawson and Whittington,¹⁵ with the British Army, had 17 fatal cases of the disease, of which 2 were due to pneumonia. In 4 of the 17 cases the pulmonary complications were so severe as to predominate the clinical picture. Here again the *Bacillus paratyphosus B* death-rate was four times as great as that of the type *A*. A most important contribution to this phase of the disease has been made by Minet.¹⁶ While working back of the French lines he was able to isolate and cultivate the *Bacillus paratyphosus* from the sputum in 7 cases, of these 4 were *Bacillus paratyphosus A*, 2 were *Bacillus paratyphosus B* and 1 was due to Gärtner's bacillus. In these cases the sputa were collected from intermittent bronchitis patients. In all cases the condition dragged along for several months, associated with emaciation, resembling chronic pulmonary tuberculosis. In one patient the condition localized itself to one apex of the lung, making its resemblance to tuberculosis still greater. Of great interest is the fact that one patient infected with *Bacillus paratyphosus B* who had completely recovered, contracted a *Bacillus paratyphosus A* infection by lounging upon the bed of an *A* type bronchitis patient. All cases under observation recovered.

Recently we have had admitted to our service at the Philadelphia Hospital a man, aged nineteen years, with a history of headache, diarrhea, general weakness and loss of weight. Examination showed the presence of herpes labialis, rose spots and an enlarged

¹³ Macroscopic Study of Lesions Produced in Paratyphoid Fever, Arch. de méd. et pharmacie Militaires, 1916.

¹⁴ Arch. de méd. et pharmacie Militaires, 1916.

¹⁵ Quart. Jour. Med., London, 1916.

¹⁶ Bull. de l'Acad. de méd., Paris, 1916.

spleen; temperature 103° F., pulse 100, respirations 28. A Widal reaction for *Bacillus typhosus* was negative. Four days after admission the patient's respiratory rate increased and he began to cough. At this time the sputum was very tenacious and blood-streaked. Remembering our experiences in the past with this type of case we immediately suspected a paratyphoid infection. The Widal reaction that day for *Bacillus paratyphosus* A was strongly positive. A blood culture was also positive for the same organism. The sputum was also cultured with a positive result. The *Bacillus paratyphosus* isolated from the sputum was agglutinated by the patient's serum. The pulmonary findings at this time were confined to the right lower lobe, and were bronchopneumonic. In addition to the paratyphoid bacillus in the sputum the pneumococcus was also present. The pneumonia, here again as in all our cases, was of short duration, lasting only four days. The patient at this time also had a series of small abscesses. The pus from these was cultured, but we were unable to isolate the bacillus. A few days after the subsidence of the pneumonia the patient developed a thrombophlebitis of the right leg, extending up to and including the external iliac vein. After the fever had subsided the pulse remained extremely rapid, ranging from 130 to 150 per minute. Soon after his thyroid became enlarged and at present there is an exophthalmos and a positive von Graefe. The Goetsch adrenalin test was applied with a positive result.

This case is of interest in showing that this disease can be as severe as a true typhoid fever, and that all complications of the latter disease can be found in association with paratyphoid fever. It also indicates that the sputum and nasal secretions of these cases should be collected and disinfected the same as the stools and urine. In a ward the possibility of cross-infections by means of cough must be borne in mind. In all cases in which the pulmonary symptoms are masked by an underlying condition the bacteriological examinations should always include those for the *Bacillus paratyphosus*.

In going over the records for the past five years at the Philadelphia General Hospital we found 15 cases of paratyphoid fever which had been diagnosed bacteriologically. Of these 4 were type A and 11 were type B infections. The pulmonary complications were as follows: Lobar pneumonia, 1; bronchopneumonia (lobar in distribution), 3; bronchopneumonia (lobar in type), 1; acute bronchitis (severe), 1; acute bronchitis (mild), 2; dry pleurisy, 1; complicated by pulmonary tuberculosis with tubercle bacilli in the sputum, 1; no pulmonary complications, 5. Seasonal variations cannot account for the pulmonary complications, as 3 of the bronchopneumonias were admitted during the mid-summer months. The shortest duration of the fever was nine days and the longest sixty-five days (a case complicated with

bronchopneumonia and a severe purulent otitis media). The age of the patients varied from fourteen to thirty-nine years. There was one death in the series, but no autopsy was made. This was due to a B. type of infection.

In conclusion, there seems to be a definite pulmonary form of paratyphoid fever which may be easily mistaken for any of the acute respiratory infections. The pulmonary symptoms and findings often precede any intestinal manifestations. Of the pulmonary complications, bronchopneumonia is the most alarming. As it has been shown that the bacilli are found in the sputum, we must recognize that bronchial infection may result in the patient becoming a chronic carrier as well as being a means of spreading the infection in the wards of a hospital. It is of interest to note that the bacilli have also been isolated from the purulent discharges of a chronic purulent otitis media, caused by other infections previous to the paratyphoid disease and that they were found as late as sixty-five days after the beginning of the illness. The organisms were also isolated from the secretions of a pyorrhea alveolaris. In view of Minet's findings and his ascribing the paratyphoid bacillus as the etiological factor in his cases of chronic bronchitis, it is worth while to examine the sputum of certain types of our chronic pulmonary invalids for this group of bacilli.

We wish to express our thanks to Dr. Joseph Sailer for the privilege of reporting two of the cases, as they occurred upon his service in the Philadelphia General Hospital.

A CASE OF PURPURA DURING SERUM DISEASE.¹

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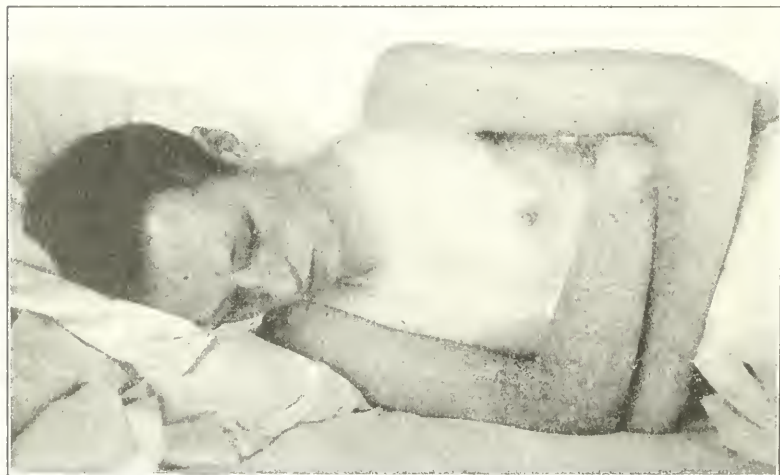
THE following case of purpura which occurred during the course of serum disease following the use of antipneumococcus I horse serum in pneumonia is of such rare occurrence as to warrant its being reported.

S. M., Austrian, aged twenty years, clerk, was admitted to the Presbyterian Hospital on February 16, 1917, complaining of pain in the left chest, with chills and fever. The onset had been sudden the night before, with headache, cough, bloody sputum and vomiting. His family history was negative for chronic illnesses. He had had

¹ From the wards of the Presbyterian Hospital, New York City.

measles as a child but no other infectious diseases. He had never been given antitoxin of any kind. Three years before he had come to the Presbyterian Hospital dispensary because of the loss of twenty-five pounds in weight, with cough and night-sweats. No physical signs of tuberculosis were found in the lungs and no tubercle bacilli were found in the sputum. He had rapidly regained his lost weight and had been well until the present illness, except for an attack of "indigestion" six months before. There was no history of bruises, epistaxis, hematuria, bloody sputum, blood in the stools or skin eruptions.

On physical examination he was found to have consolidation of practically the whole left lower lobe. Cheeks were flushed, breathing was rapid and grunting, with frequent cough and glairy, bright red sputum. His heart was normal except for a rough systolic murmur localized to the pulmonic area. His abdomen was not distended. There was no skin eruption. Temperature 104.6° F., pulse 112 and respirations 34. Examination of the blood showed 21,600 white blood cells, with 90 per cent. polymorphonuclear leukocytes. Blood culture gave no growth of bacteria. The sputum was injected into a mouse, from which was recovered pneumococcus Type 1.



Purpura occurring during serum disease. Note intensity of eruption below point of constriction of right arm by tourniquet.

Intra-cutaneous tests were performed with horse serum, using human serum and carbolyzed saline as controls. All were negative. One hundred cubic centimeters of antipneumococcus serum obtained from the Rockefeller Institute was given intravenously, diluted with 100 c.c. of normal saline. The patient experienced a slight chill, with dyspnea, which was relieved by atropin and adrenalin

given subcutaneously. His temperature rose from 101° to 105° and then fell gradually to 102° in the next eight hours. At that time another 100 c.c. of serum were given, with no discomfort to the patient. His temperature continued to fall, reaching 100° twelve hours later, when a third dose of serum was given. The following day his temperature was 98.6° , white blood cells 6100 with 77 per cent. polymorphonuclear leukocytes. The physical signs suggested the presence of free fluid in the left chest, which roentgen ray failed to confirm. Four days later exploration of the left chest recovered 10 c.c. of bloody fluid, which showed no organisms on smear and no growth on aerobic and anaerobic culture.

Seventh Day after First Serum Administration. A general slight enlargement of the lymph nodes appeared, with patches of erythema and urticaria scattered over the skin and numerous minute bright red petechial hemorrhages over the chest.

Tenth Day. The urticaria persisted, the lymph nodes were much enlarged and the inguinal nodes were quite tender. Face and eyelids were puffy. Patient complained of pain in both temporomandibular joints, in both shoulders and in the joints of both hands.

Eleventh Day. Patient complained of pain in all joints of his extremities except his ankles and feet. There was general slight swelling of all extremities. There was a diffuse papular erythema of the whole body. There was marked conjunctivitis in both eyes. A few urticarial wheals and new petechial spots were present. Temperature rose to 102.4° . The patient's blood showed the presence of precipitins for horse serum.

Twelfth Day. Throat was sore and diffusely red. Patient coughed up a little blood-tinged mucus. White blood cells were 13,600, with 87 per cent. polymorphonuclear leukocytes.

Thirteenth Day. Temperature, 104° . Cervical and inguinal nodes tender. At night the patient had a severe epistaxis, which was checked only by packing both anterior and posterior nares.

Fourteenth Day. Erythema somewhat faded, but many minute petechial spots appeared over thighs and chest. After the application of a tourniquet to the right arm above the elbow for venous puncture, a profuse purpuric eruption appeared all over the arm below the point of constriction. Skin and mucous membranes were now quite pale. Joint pains practically gone. Blood platelets, 315,000 per c.mm. Normal control, 330,000. Bleeding time, two minutes. Coagulation time, six minutes. Normal control, seven minutes. White blood cells, 10,600, with 83 per cent. polymorphonuclear leukocytes. Urine showed a faint trace of albumin and a negative guaiac test for blood.

Fifteenth Day. Petechial hemorrhages were present all over the body and in the mucous membranes of the mouth. There were several large submucous hemorrhages in the soft palate, probably

caused by trauma in packing the posterior nares. The lymph nodes were still quite tender. Erythema still present as well as a few new urticarial wheals. The spleen was palpable for the first time. Ophthalmoscopic examination revealed no hemorrhages in the choroid.

Sixteenth Day. Fresh petechial spots present on the shoulders and along scratch marks on the back. Red blood cells, 3,700,000; hemoglobin, 80 per cent. White blood cells, 6600; polymorphonuclear leukocytes, 79 per cent.

Seventeenth Day. Petechial eruption more extensive. Gums bleeding slightly. Spleen no longer palpable. Dark blood passed with a stool. Temperature, 101.6° to 103.4°.

Twenty-first Day. Temperature normal. General condition much better. Purpuric eruption gone except on buttocks and thighs. No more joint pains. Lymph nodes, especially one in the submaxillary region, still large but not tender.

Twenty-fifth Day. Temperature suddenly rose to 103.8°. Patient complained of difficulty in breathing and of very sore-throat. Swallowing very difficult, permitting the taking of fluids only. A hemorrhagic area was present on the left tonsil.

Twenty-sixth Day. Slight epistaxis. Petechial hemorrhages have all disappeared from the skin. Tourniquet applied to right arm for ten minutes produced no purpuric eruption. Lungs clear except for a few dry, inspiratory rales at the left base. Red blood cells, 4,300,000; hemoglobin, 60 per cent.; white blood cells, 19,000; polymorphonuclear leukocytes, 84 per cent.

Twenty-seventh Day. Nose and throat examined by Dr. Coakley. There was an area of ecchymosis on the right side of the nasal septum and on the right lower turbinate, possibly from the packing. The uvula was edematous, with diffuse capillary hemorrhages on the posterior surface. These extended to the posterior pillars of the fauces, which were very edematous. The anterior pillars were less so. Fresh blood was leaking from the left lateral pharyngeal wall, the point of origin not being visible. The epiglottis was very edematous on the left side, involving the left arytenoid cartilage. There was an ecchymotic area on the upper surface of the epiglottis. The vocal cords were congested.

Twenty-ninth Day. Slight epistaxis occurred. Another new petechial spot. Throat less edematous. Temperature rose in the afternoon to 104.6°. For the past few days every stool had contained either streaks or clots of blood.

Thirtieth Day. Temperature normal. Patient transferred to the hospital roof and felt much better.

From this time on the temperature continued normal and convalescence was rapid. No more petechial hemorrhages appeared and no more blood appeared in the stools. The swelling of the throat rapidly disappeared and the lymph nodes returned to their normal size.

Thirty-sixth Day. Precipitins for horse serum still present in patient's blood.

Thirty-seventh Day. Red blood cells, 4,100,000; hemoglobin, 60 per cent.; white blood cells, 9100, polymorphonuclear leukocytes, 61 per cent.

Fortieth Day. Patient discharged.

DISCUSSION. Schultz,² in discussing "Anaphylactoid Purpura," mentions three cases reported by Widmer³ in which "purpura simplex" followed the administration of diphtheria antitoxin to small children. The only other case of purpura following the administration of serum, which we have been able to find in the literature is one reported by Flandin,⁴ in which the subcutaneous administration of one dose of diphtheria antitoxin was followed thirteen days later, when the patient got up, by edema of the legs, arthritis with effusion, urticaria, erythema and purpura. The symptoms disappeared after rest in bed but recurred each time the patient got up. Calcium chloride and peptone injections had no effect on the recurrences, but finally minimal doses of normal horse serum (0.1 to 0.2 c.c.) given hypodermically, rapidly dispelled the symptoms. After this they reappeared mildly every two or three months and were each time relieved by small doses of horse serum. Each time the symptoms recurred the patient's blood serum was found to be toxic for a guinea-pig. After the injection of horse serum, however, this toxicity disappeared.

The occurrence of purpura during the course of these cases of serum disease seems to link serum disease etiologically more closely with the group of conditions commonly known as idiopathic purpura. The type of purpura observed in our case is not that which is characteristic of purpura hemorrhagica where there is a marked decrease in the number of blood platelets and where the bleeding time is greatly prolonged. (Platelets and bleeding time were both normal in our case.) But all these cases showed many of the features of the purpura which appear as a secondary manifestation of some of the acute infectious diseases or which occurs without any demonstrable cause or any abnormality of the blood elements. Osler⁵ has followed many of these cases through varied manifestations of the disease, extending over many years and with several distinct attacks, some of which were associated with joint pains, some with abdominal pains, erythema, urticaria or even angio-neurotic edema. Sometimes the purpura itself did not appear but the same pathological condition was suggested by the appearance of the other symptoms.

In the case reported we have the symptoms of both purpura

² *Ergeb. d. Inn. Med. u. Kinderheilk.*, 1919, xvi, 32.

³ *Med. Klin.*, 1917, Nr. 39.

⁴ *Bull. et mém. Soc. méd. des hôp.*, 1914, xxx, 242.

⁵ *British Med. Jour.*, 1914, i, 517.

and serum disease and we have a known foreign substance in the blood and tissues (horse serum), which, either by its own presence or by the attempt of the patient to eliminate it, may be safely inferred to be etiologically associated with all of the symptoms. In our case there is considerable evidence that the purpuric eruption was due not to any abnormality of the blood but to some temporary lesion of the finer bloodvessels. The most marked eruptions occurred in regions which were most exposed to trauma, namely, the nasal and pharyngeal mucosa, the extensor surfaces of the arms, especially about the elbows, the buttocks, along scratch marks on the back, and especially on the arm below the site of constriction by a tourniquet which shut off the venous return and thereby caused distention of the capillaries. On the other hand, in places like the conjunctiva and retina, where trauma is not likely to be a factor, no hemorrhages occurred.

Bloodvessel lesions have been found in some experimental conditions in which capillary hemorrhages occurred. Gay and Southard⁶ in their early studies in anaphylaxis found hemorrhages in the gastric mucosa, lungs, spleen, heart muscle, brain and several other organs of sensitized guinea-pigs, which had died of anaphylaxis following a toxic dose of horse serum. Associated with the hemorrhages they found focal fatty infiltration of endothelial cells of the capillaries. Flexner and Noguchi,⁷ and later Pearce,⁸ in studying snake-venom poisoning, also found lesions of the capillary endothelium associated with hemorrhages into various organs. The lesions here, however, were not fat infiltrations, but a swelling and lysis of the endothelial cells occurring focally and allowing extravasation of blood into the surrounding tissue. A third type of lesion of the capillary endothelium, which has been suggested as a possibility, from the result of a toxin introduced into the blood, is the dissolution of the so-called intercellular cement substance of the capillary endothelium, with extravasation of blood between the separated cells.

As no tissue from these cases was secured for microscopic examination the type of lesion in the capillaries, if one existed, can only be conjectured. In our case it is probable that any lesion which did occur was only temporary and lasted only as long as the effects of the toxic substance in the body continued. This is suggested by the fact that after the subsidence of the symptoms the application of a tourniquet to the arm no longer produced a purpuric eruption, as it had done during the height of the disease. The capillaries were again able to stand distention without rupturing. In Flandin's case, however, the lesion seems to have been much more permanent, for the symptoms recurred at intervals for an indefinite period and

⁶ Jour. Med. Res., 1907, xvi, 143.

⁷ Univ. Penna. Med. Bull., 1902, xv, 345.

⁸ Pearce, R. M.: Jour. Exper. Med., 1909, xi, 532.

were only temporarily relieved by treatment. The toxicity of the patient's serum for a guinea-pig in his case seems to point to the production of a circulating toxin which periodically caused the appearance of the symptoms. Whatever the mechanism the evidence at hand suggests that the cause of some cases of purpura whose etiology is now so obscure may some day be demonstrated to be an intoxication following the introduction of a foreign protein into the body and therefore similar to the intoxication causing serum disease.

SUMMARY. 1. A case is described in which purpura occurred during the course of serum disease following the administration of *antipneumococcus horse serum.

2. The elements of blood coagulation were normal, and it is therefore probable that the purpura was due to the presence of a toxin associated with the attempt of the body to eliminate the foreign protein.

3. The evidence points to the capillary walls as the site of the lesion.

4. Some cases of purpura of unknown etiology may be caused by the same type of intoxication which was present in this case.

PROGNOSTIC FACTORS IN PNEUMONIA DURING THE INFLUENZA EPIDEMIC.

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THE title of this paper is purposely evasive. It speaks of "the influenza epidemic" because it is by that term that the disease which swept the world nearly a year and a half ago is generally known. In adopting the term it is with the mental reservation shared by many others as to the primary etiological factor. What part the *Bacillus Pfeiffer* played is difficult to judge from the widely varying reports of equally skilled observers. It is not within the scope of this paper to discuss that question.

Again, many patients suffered at that time from the disease known as influenza without having a complicating pneumonia. On the other hand we know that the outstanding cause of death during the epidemic was an inflammatory affection of the lungs generally referred to as "pneumonia." When patients were seen at varying periods of their illness it was often—indeed usually—impossible to be sure that existing pneumonia had been ushered in by influenza. This uncertainty is expressed by the phrase "pneumonia occurring during the influenza epidemic."

It seems desirable to include a consideration of lobar pneumonia as well as the bronchial type, since a fair percentage of cases of the

lobar variety occurred during the epidemic, and necessarily, therefore, enter into the question of prognosis.

On this basis it is believed the situation can be reviewed in the light of the conditions that actually prevailed.

During the fall of 1918, Base Hospital 45, located at Toul, France, received 3965 cases diagnosticated as influenza or pneumonia. These affections seemed to agree in their main features with the pandemic disease prevailing at that time. As regards bacteriology the observations at this hospital align themselves with those reporting negatively as to any apparent role of the *Bacillus pfeiffer* as the causative agent of pneumonia. They agree with the frequently expressed opinion that, the question of primary etiology aside, the complicating pneumonia is attributable largely to streptococci and to a lesser extent to pneumococci, and that the mortality is attributable largely to the streptococcus, especially *Streptococcus hemolyticus*.

While circumstances necessarily affected the character of clinical studies made in the cases, the data are fairly complete in the series of 67 cases used as the basis for this report, and they may be accepted as representative of the larger number not included for lack of recorded data. No cases of pneumonia complicating gas inhalation are included. Our present purpose is to examine these 67 cases as to clinical, radiographical and postmortem features, with a special view to determining prognostic factors.

For purposes of discussion certain terms are used in connection with bronchopneumonia which will be defined. Clinically, on the basis of physical signs and roentgen-ray pictures, three varieties of bronchopneumonia will be referred to:



FIG. 1.—Illustrating the type of bronchopneumonia defined as "discreet."

DISCREET. To denote by physical signs limited, well-defined patches of pneumonia, few in number and of no great extension; and the same by the roentgen ray (Fig. 1).

DIFFUSE. Giving widely distributed signs, chiefly rales, bilateral, with no large areas of consolidation, showing by the roentgen-ray numerous, widely distributed, small areas of consolidation or diffuse, very small areas of consolidation closely resembling military tuberculosis (Fig. 2).

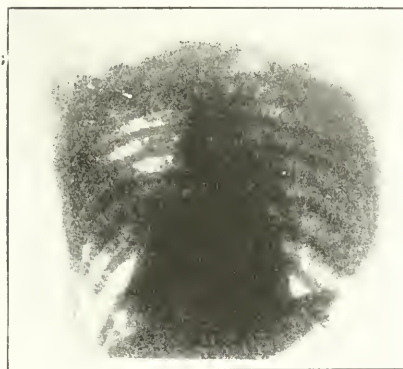


FIG. 2.—Illustrating the type of bronchopneumonia defined as "diffuse."

CONFLUENT. Showing by physical signs and roentgen-ray shadows widely distributed lesions, usually bilateral, not sharply defined, including on one side or both massive areas of consolidation (Fig. 3).

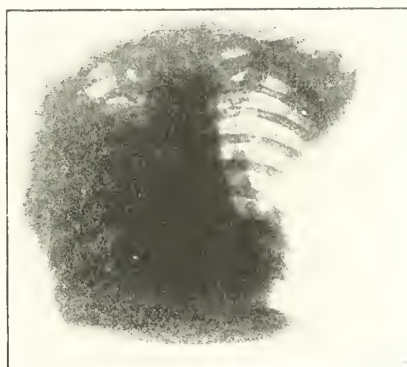


FIG. 3.—Illustrating the type of bronchopneumonia defined as "confluent."

The definitions are somewhat arbitrary. There was no sharp dividing line between the types. That kind of case designated "discreet" was clearly separable from the "confluent." But in an endeavor to separate an intermediate group, the "diffuse," borderline cases are encountered. In the two cases diagnosticated "diffuse" which died, confluent lesions were demonstrated at autopsy.

In contradistinction to all of these stands lobar pneumonia (Fig. 4), with its clear-cut, anatomical limitations, both to physical examination and the roentgen ray. And yet, even here, it is certainly possible to have a mixed type of infection, with a genuine lobar involvement and more or less of the bronchial type in other portions of the lung. Such is believed to have been the real condition in Case 33 of the series, which, in its clinical course, gave very strongly the impression of a frank, lobar pneumonia, yet on physical examination and roentgenologically has to be grouped as a confluent bronchopneumonia.



FIG. 4.—Illustrating lobar pneumonia.

Following is the descriptive postmortem pathology based on the report of Dr. Jean Oliver, who performed the autopsies in these cases as part of a series of 103.

The cases of lobar pneumonia differed in no way from the text-book description.

The few cases of acute interstitial pneumonia (McCallum) and of bronchopneumonia of the text-book variety seen at autopsy included no cases of this series.

On the other hand the postmortem pathology corresponding to the antemortem descriptive term "confluent" was nearly constant, and has been called "hemorrhagic bronchopneumonia," "hemorrhagic necrotizing bronchopneumonia," or "hemorrhagic pneumonitis." As this was the type found at postmortem in nearly all the cases of our series, an abstract of the description is given as follows:

In the newer lesions the prevailing picture was one of intense hyperemia and edema. Bloody fluid poured out of the sectioned lung, which was firm and doughy, especially posteriorly. At this stage there was little or no true consolidation.

Later a process of consolidation is added. Even the consolidated area is still very moist and indefinite. It runs in irregular bands through the lung tissue, leaving edematous areas still containing

air, the cut surface presenting a yellowish-gray appearance, streaked with the red or almost black hemorrhage of the earlier stage. Brownish-yellow pus now exudes from the lung tissue. There may be isolated areas of sharper outline and firmer consistency, which are really infarctions. Later still these isolated areas especially tend to undergo necrosis or the formation of abscesses from 1 to 5 cm. in diameter.

The bronchi are filled with pus, the mucous membrane undergoing destruction. The trachea is not usually involved except for hyperemia. The peribronchial lymph nodes are swollen, hemorrhagic or may contain abscesses.

The pleura is at first smooth and glistening, with more or less hemorrhage. Following this an exudation of fibrin occurs and in some cases a thin brownish-yellow pus develops.

Microscopically the infection is seen to originate chiefly in the smaller bronchi.

While the above description emphasizes the striking condition of hyperemia and edema, it should not be forgotten that practically all cases showed a considerable amount of consolidation or near-consolidation, especially in the posterior portions of the lungs, that could usually be detected clinically as areas of increased density.

The character of the lesion was liable to declare itself early. Except for the more intensive "diffuse" cases, already referred to as borderline, there was little or no tendency of lesser lesions to become transformed into the graver type. It is plain that on the accuracy of this statement depends very largely the value of the others. In its support are offered the consecutive physical and roentgen-ray examinations made in individual cases, especially the radiographic evidence.

On the basis of physical examinations and in most cases roentgen ray reports of the 67 cases were distributed as follows:

TABLE I

Bronchopneumonia:	Cases.	Deaths.
Discreet	15	0
Diffuse	19	2
Confluent	15	13
Lobar pneumonia	12	1
Negative as to pneumonia	6	0
Total	67	16

There was a total of 16 deaths, or 26 per cent. mortality, in the pneumonia cases. Of the 16 deaths 13 were recognized clinically as confluent; 2 were regarded as diffuse, but were in reality confluent by the time they came to autopsy at least. One was lobar pneumonia complicated by empyema and peritonitis. No discreet case died. Thus it is seen it was the exception for any confluent case to get well and the exception for any other type to die.

TEMPERATURE, PULSE AND RESPIRATION. Next to the determination of the confluent type of bronchopneumonia a rapid respiratory rate (with cyanosis) in the presence of bronchopneumonia was a particularly ominous sign (Table II). Taking as a standard a respiratory rate of 40 or over, maintained for two days or more, 10 of the confluent cases had such a respiration, with 9 deaths. The 2 diffuse cases which died also breathed in this way. Altogether there were 17 in this class, with only 5 recoveries, and 3 of the recoveries were patients with lobar pneumonia. The respiratory rate did not, therefore, seem to have the same significance in lobar pneumonia as it had in bronchopneumonia.

TABLE II

Respiration over 40:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Fatal	0	2	9	1	0	12
Non-fatal	0	1	1	3	0	5
Respiration 40 or under:						
Fatal	0	0	4	0	0	4
Non-fatal	15	16	1	8	6	46
Total	15	19	15	12	6	67

The temperature (Table III) furnished no prognostic indications comparable with the respiration, nor did the pulse. Thirty-four cases ran a temperature over 101°, and of the 11 deaths in this class 9 were of the confluent type.

TABLE III

Temp. over.	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
104°—Fatal	0	1	9	1	0	11
Non-fatal	7	5	2	6	3	23
103°—Fatal	0	1	4	0	0	5
Non-fatal	6	7	0	5	1	19
102°—Fatal	0	0	0	0	0	0
Non-fatal	2	3	0	0	1	6
101°—Fatal	0	0	0	0	0	0
Non-fatal	0	2	0	0	1	3
Total	15	19	15	12	6	67

Of the 16 cases that died only 8 had a pulse-rate over 120, at least not until moribund. A pulse slow in proportion to temperature was generally seen and postfebrile bradycardia was pronounced in 15 cases.

TABLE IV

Chill:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Fatal	0	1	3	1	0	5
Non-fatal	7	7	0	7	2	23
No chill:						
Fatal	0	1	5	0	0	6
Non-fatal	8	10	0	4	4	26
Total	15	19	8	12	6	60

CHILL AND HEMOPTYSIS. Positive or negative record of chill was made in 60 cases (Table IV). Twenty-eight cases had chill; 32 had not. The mortality in the former was 18 per cent. In the latter 23 per cent., a difference of no significance.

With regard to hemoptysis the record (Table V) showed 27 positive with 30 per cent. deaths, and 35 negative with a death-rate of 11.5 per cent. The difference here seems great enough to be regarded, especially when it is noted that in the group not showing hemoptysis none died except the confluent type. At the same time either cyanosis, abdominal distention or jaundice was regarded a graver sign than hemoptysis.

TABLE V

Hemoptysis:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Fatal	0	2	5	1	0	8
Non-fatal	5	8	1	5	0	19
No hemoptysis:						
Fatal	0	0	4	0	0	4
Non-fatal	10	9	0	6	6	31
Total	15	19	10	12	6	62

SPUTUM BACTERIOLOGY. Using the Avery method the sputum was examined in 52 cases (Table VI).

TABLE VI

Pneumococcus:	Cases.	Fatal.
Type I	3	0
Type III	1	0
Type IV	26	6
Types I and II	1	1
Type II and hemolytic streptococcus	1	0
Type IV and hemolytic streptococcus	1	1
Type IV and non-hemolytic streptococcus	2	0
Type IV and undetermined streptococcus	1	1
Hemolytic streptococcus	4	2
Non-hemolytic streptococcus	11	1
Non-hemolytic streptococcus and Bacillus influenzae	1	0
	52	12

The Bacillus influenzae was demonstrated only once and then in combination with a streptococcus. The results in all other cases were a pneumococcus or streptococcus or a combination of both. The sputum bacteriology had to be considered of little or no prognostic value, for in the first place it had no relation to the type of pneumonia (Table VII).

Streptococci alone were found in the sputum of lobar cases, and pneumococci (chiefly Type IV, it is true) were found alone in many of the bronchial type. This is not to say whether or not the streptococcus can produce a true lobar pneumonia. It does make questionable the value of such sputum examinations under the conditions being discussed.

TABLE VII

Pneumococcus:	Disc.	Dif.	Conf.	Lobar.	Neg.	Total.
Type I	0	1	0	2	0	3
Type III	0	0	0	1	0	1
Type IV	8	5	6	3	3	25
Types I and II	0	0	0	1	0	1
Type II and hemolytic streptococcus	0	0	1	0	0	1
Type IV and hemolytic streptococcus	0	0	1	0	0	1
Type IV and non-hemolytic streptococcus	1	1	0	0	0	2
Type IV and undetermined streptococcus	0	0	1	0	0	1
Hemolytic streptococcus	2	0	1	0	1	4
Non-hemolytic streptococcus	2	5	1	3	0	11
Non-hemolytic streptococcus and Bacillus influenzae	0	0	0	1	0	1
Undetermined streptococcus and tubercle bacilli	0	0	1	0	0	1
Non-hemolytic streptococcus and tubercle bacilli	0	1	0	0	0	1
Total	13	13	12	11	4	53

The fact that in these cases the organism reported as predominating in the sputum bore no relation to the type of pneumonia is clearly indicated by Chart I. The curves for pneumococci and for streptococci alone or in association with other organisms correspond very closely to the base line indicating the relative incidence of the different types of pneumonia.

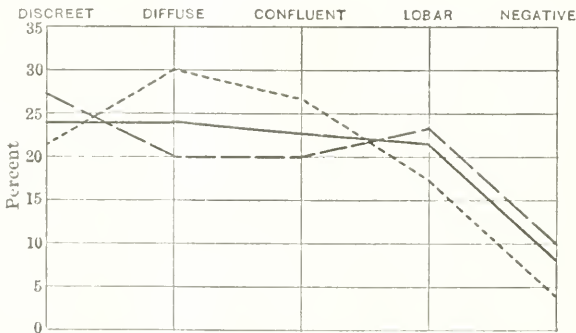


CHART I.—Base line ———, 53 cases. Pneumococci alone ———, 30 cases. Streptococci alone (15 cases) and with pneumococci (5 cases) or other organisms (3 cases) -----.

Again (Table VIII) in each case cultured at postmortem (12 cases) a streptococcus was recovered from the lung tissue, a Strepto-

coccus hemolyticus nine times, whereas it had been found in the sputum of only 2 of these 9 cases. It should be stated, however, that in 3 of these 9 cases the sputum had not been examined.

TABLE VIII

Case No.	Sputum bacteriology.	Lung bacteriology at autopsy.
2	Pneumococcus, Type IV; streptococcus undetermined	Non-hemolytic streptococcus.
3	Hemolytic streptococcus.
4	Pneumococcus, Type IV	Hemolytic streptococcus.
5	Pneumococcus, Type IV; hemolytic streptococcus.
7	Pneumococcus, Type IV; hemolytic streptococcus	Hemolytic streptococcus.
15	Non-hemolytic streptococcus (same in antemortem blood).
16	Non-hemolytic streptococcus	
21	Hemolytic streptococcus	Hemolytic streptococcus.
25	Bacillus tuberculosis	
29	Pneumococcus, Type IV	Hemolytic streptococcus (undetermined streptococcus in antemortem pleural fluid).
47	Hemolytic streptococcus.
53	Pneumococcus, Types I and II	Hemolytic streptococcus.
60	Pneumococcus, Type IV	
61	Pneumococcus, Type IV	Non-hemolytic streptococcus; Bacillus influenzae.
62	Pneumococcus, Type IV	Hemolytic streptococcus.
63	Pneumococcus, Type IV	

BLOOD CULTURES. Blood cultures were made in 54 cases, of which only 3 were positive. Each of these gave a non-hemolytic streptococcus. Two had been diagnosticated diffuse bronchopneumonia and one lobar pneumonia. One of the so-called diffuse cases (really confluent) died, the other and the case regarded as lobar pneumonia got well. The blood cultures and sputum ran truer to each other than did the postmortem lung bacteriology and sputum. Of the three non-hemolytic streptococcic blood cultures two had shown the same organism in the sputum, while in the third the sputum was not examined. With so small a percentage of positive blood cultures manifestly this procedure was of no value in prognosis. A larger number of positive results might have been obtained if repeated attempts had been made in individual cases. More than one culture was made in only a few cases.

BLOOD COUNTS. Blood counts were made in 62 cases (Table IX).

A count under 10,000 was obtained in 45 cases, with 12 deaths (27 per cent.), and a count above normal in 17 cases with 3 deaths (18 per cent.). A leukocytosis did not point to recovery when it occurred in the confluent type and a low or normal count was not often of bad prognostic import in other types.

BLOOD-PRESSURES. Blood-pressures were recorded in 55 cases (Chart II). On the basis of a single reading taken at the height of illness the systolic pressure was slightly higher in the fatal cases

than in the non-fatal, the systolic relatively higher than the diastolic, giving a slightly wider pulse-pressure in the fatal cases, an average

TABLE 1X

	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Under 5000:						
Fatal	0	0	0	0	0	0
Non-fatal	2	3	0	1	0	6
5000 to 10,000:						
Fatal	0	2	9	1	0	12
Non-fatal	10	9	1	3	4	27
10,000 to 15,000:						
Fatal	0	0	1	0	0	1
Non-fatal	0	2	0	3	1	6
Over 15,000:						
Fatal	0	0	2	0	0	2
Non-fatal	3	1	1	3	0	8
Total	15	17	14	11	5	62

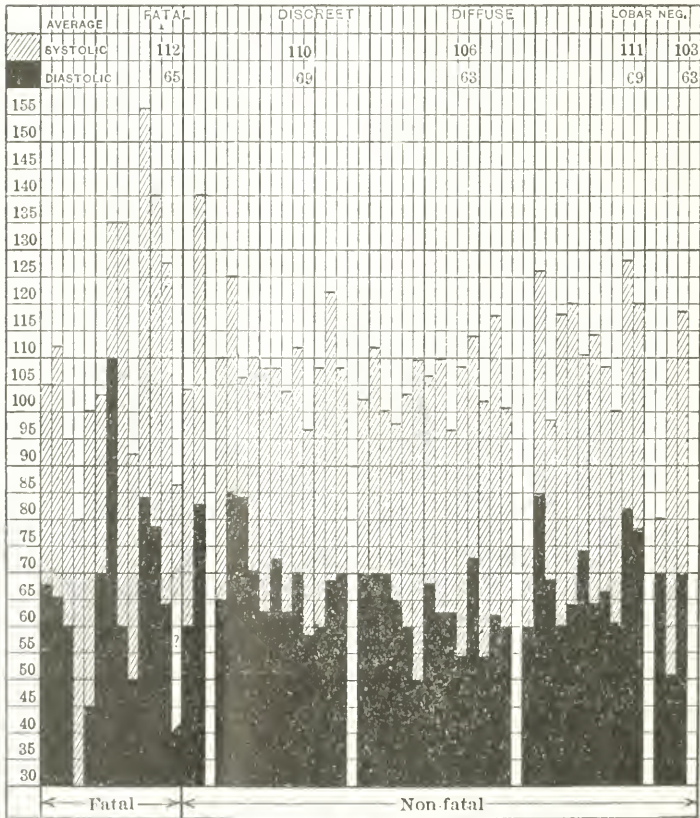


CHART II

of 47 as against 40 to 43 in the different types of non-fatal cases. There was less uniformity in the readings of the fatal group. There were no differences of value in prognosis. In general the averages were slightly lower than normal for men between the ages of twenty-one and thirty-one years.

In 8 non-fatal cases in which subsequent readings were recorded during convalescence there was an average systolic gain of twelve points, and an average diastolic gain of fifteen points. In 4 fatal cases in which subsequent readings were recorded before death they also showed an average gain of seven points systolic and nineteen points diastolic. No explanation of this unexpected finding is attempted.

TABLE X

	Fatal.	Non-fatal.
Empyema and meningismus in bronchopneumonia	Case 26	
Empyema in bronchopneumonia and pulmonary tuberculosis	" 23	Case 29
Empyema and peritonitis in lobar pneumonia	" 50	
Empyema in lobar pneumonia	" 50	" 6
Primary diarrhea and gross urinary findings	" 44	
Septicemia (non-hemolytic streptococcus)	" 15	Cases 18, 21
Membranous tonsillitis, purulent conjunctivitis and ulcerated foreskin	..	Case 1
Follicular tonsillitis	..	" 10
Otitis media	..	" 12
Primary dysentery	..	" 13
Abscess cellular tissue of back	..	" 62
Ischiorectal abscess	..	" 33
Syphilis	..	" 22
Recrudescence	..	" 45

COMPLICATIONS. The most frequent complications were empyema and pulmonary tuberculosis (Table X). In 2 cases only was the complication believed to be an important factor in the fatal termination, 1 of bronchopneumonia complicated by pulmonary tuberculosis and empyema, and 1 of lobar pneumonia, with a late complicating empyema and peritonitis. Subcutaneous emphysema was seen four or five times in the cases admitted to the hospital during the period under discussion, but did not occur in the series here included. Unusually gross urinary findings were reported in one case only of the series. This case died, but the kidneys were reported not grossly diseased at autopsy.

In the matter of race no differences in mortality were noticeable between white and colored troops. Deaths were about proportionate to incidence in the two races. The patients were all males, and age does not enter as a factor, as the men were all between the ages of twenty-one and thirty-one years.

It would be natural to inquire whether treatment did not play a part in the prognosis of these cases. Conditions of exposure and bodily exertion prior to entrance into a Base Hospital; distance of transportation and similar factors were, no doubt, highly significant.

After reaching the Base Hospital, from which the patient need not be evacuated until his condition warranted, the treatment carried out was essentially the same in all cases, being almost entirely symptomatic except for operations for empyema.

SUMMARY. It is desired to emphasize certain simple bedside standards of prognosis because the other data seem to be less significant as to the outcome in a given case.

The fatal type of pneumonia occurring in this series as seen at autopsy was that to which the name hemorrhagic bronchopneumonia or hemorrhagic pneumonitis has been applied.

This type could usually be recognized clinically as a confluent bronchopneumonia, bilateral, with evidence of considerable consolidation, yet the consolidation not of a frank lobar type. It was usually characterized by a respiratory rate of forty or over for a period of two days or more, and this rate was rarely seen in bronchopneumonia of other grades. Cyanosis was usually proportionate to the respiratory rate.

In lobar pneumonia a rapid respiratory rate was not so significant.

The roentgen ray was of great assistance in locating and defining small areas of pneumonia, in determining the presence or absence of fluid and other complications, but it was usually not essential to the diagnosis of the confluent type.

In conclusion, the data presented may be summarized in a very simple statement. Having recognized the existence of a bronchial type of pneumonia as distinguished from a lobar type, the question of prognosis seemed to be largely a matter of the density and extent of the pulmonary lesions.

My thanks are due Dr. Fred M. Hodges for the roentgen-ray studies and Dr. E. Guy Hopkins for the clinical laboratory data.¹

THE TREATMENT OF ACUTE GONORRHEA IN FEMALES.

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IN the very beginning of this paper it is my desire to state that I have no new method of treatment to offer, I have not discovered a "sure cure" for gonorrhoea and I have no criticism to make of the many methods of treatment now in vogue. However, a close relationship with undergraduate medical students for several years has

¹ The detailed clinical data and abstracts of the physical, roentgen-ray and post-mortem findings of the cases forming the basis of this report were submitted for publication, but have been omitted because of lack of space.—Ed.

brought to my attention that there is something lacking in the present teachings on the subject of acute gonorrhœa, and as nearly as I can determine the lacking element is the failure on the part of medical schools and medical authors to tell the student exactly what to do and to show him how to do it. The student attends lectures and clinics by the score, but almost invariably the subjects considered are operative conditions and technic, and it is only in very rare instances that much time is spent in discussing local treatment. Even more important is the very small opportunity that is presented to the average student to see how local treatments are applied and to actually apply them himself. It has often been truthfully stated by students that they graduate from medical schools prepared to perform a hysterectomy while they do not know how to insert a speculum into the vagina. They add little to their knowledge, as a rule, during their service as interns, and, as a result, when they take up active practise they are very poorly qualified to treat the so-called non-operative gynecological cases. An attempt has been made to overcome this state of affairs in the gynecological department of the University of Pennsylvania Medical School by giving the students practical work in the dispensary for a period of ten weeks. The course has been greatly appreciated by practically all of the students who have taken it, but in order to make it a real benefit it has been necessary to limit the classes to a few men at a time, so that only about 10 per cent. of the students have an opportunity of taking the course.

To the student or practitioner who consults such an excellent monograph as that of Norris¹ there will be ample opportunity to obtain a complete *résumé* of all that we know about the treatment of gonorrhœa, and one or two of the more recent text-books contain excellent articles on this subject; but the general tendency of authors has been to lightly skip over the acute stage of the disease and then dilate upon the chronic stage and its complications. This appears especially ludicrous in view of the fact that careful observation and treatment during the acute stage may frequently prevent the ravages of pelvic inflammatory disease. At this point I should like to mention the wrong impression that is held by the average practitioner, due, no doubt, to erroneous instruction during student days, namely, that gonorrhœa in the female is an incurable disease. In large measure this view is probably the result of Noeggerath's dictum, "Once infected, always infected," but such a statement does not hold good so long as the infecting organism has not passed into the uterine canal above the internal os. It is a common experience for the gynecologist to cure cases of acute endocervicitis, and yet the physician in general practice is always skeptical about such a report. The object of this paper, therefore, is to encourage more

¹ Gonorrhœa in Women, Philadelphia and London, 1913.

extensive instruction in the treatment of acute gonorrhœa in the female, so that the practitioner may undertake the treatment of these cases with a cheerful optimism as to the outcome, even though he may not be successful in all cases. In describing the method of treatment that has given me the most satisfaction, I shall divide the subject into acute urethritis and acute endocervicitis, since these are the most common types of infection. Acute inflammation of the vulvovaginal glands will not be considered, as it is freely admitted that it is my belief that we are unable to cure this condition without extirpating the glands, and any cases of non-operative cure that have occurred are, to my mind, not the result of any special line of treatment.

ACUTE URETHRITIS. Acute urethritis, which is usually the first stage of acute gonorrhœa, is best treated by absolute rest and no local treatment during the period of the acute purulent discharge. The average patient who suffers from this condition, however, cannot or will not remain in bed, so that we are obliged to treat them as ambulatory cases. At the dispensary of the University Hospital we give these patients two prescriptions, one for santal oil, which is taken in 10-minim doses, three times daily, and the other prescription is for a urinary sedative containing 5-minims of tincture of hyoscyamus and 10 grains of sodium bromide to 1 dram of the liquor of potassium citrate, which is taken every three hours. The patient is instructed to drink water freely and return in a week, at which time, if the acute inflammation persists, the treatment is continued in the same manner. In the course of two or three weeks most cases will show a marked improvement, as evidenced by the freedom from symptoms and the diminution or the disappearance of the urethral discharge. It is at this time and not until then that local treatment is instituted, and when the treatment is begun, the patient must be warned that freedom from symptoms does not mean freedom from disease, as there is a great temptation for the patient to discontinue treatment. We have tried many agents in the local treatment of urethritis, but have come back to the use of silver preparations, using either a 15 per cent. solution of silver nucleinate or a 5 per cent. solution of silver nitrate, which is applied to the entire length of the urethra by means of a small cotton swab on a nasal applicator. A word or two regarding details may not be amiss at this point, since close observance of the finer points in technic will determine the efficacy of the treatment.

The patient should urinate just before the treatment and then the urethra should be well dried by gently passing a dry wisp of cotton on an applicator into the urethra. This drying is important, because the power of any gonococidal agent is enormously enhanced by previous drying of the parts. The medicament is then absorbed on another cotton swab and the entire urethra is painted by means of a slow spiral movement of the applicator, which is continued until

the bladder is reached. The applicator is then withdrawn by the same spiral motion, *in the same direction*, so that the cotton is being tightened on the applicator instead of being loosened. Failure to observe this small point may result in the unpleasant accident of having the cotton caught by the internal sphincter and retained in the bladder. Although this is disconcerting to the physician it need cause no alarm, as the patient will not be aware of its presence, and, moreover, she will pass it at a subsequent urination. These treatments are given every two or three days until improvement in the local condition is noticed, and then the frequency of the treatments is gradually reduced until all signs have disappeared. At this time smears should be taken, and after three successive negative smears have been obtained a cure may be assumed.

ACUTE ENDOCERVICITIS. In considering the treatment of gonorrheal endocervicitis we should not expect quite as rapid improvement as can be obtained in the treatment of urethritis; nevertheless, by conscientious and continued treatment we shall be rewarded by results far above the expectations of the average practitioner. As soon as we have determined the presence of a gonorrheal discharge from the cervix, we order hot douches of 1 to 8000 potassium permanganate solution to be taken four or five times daily. We have found this solution to have the best cleansing effect in these cases, and if ordinary care is used, many of the objectionable features of permanganate can be obviated. We order it for our patients in the form of 1-grain tablets, which are dissolved just before use. As soon as the discharge is well under control, which ordinarily occurs in about two weeks, we begin to give the patient local treatments to the cervical canal. In applying any medicated solution to the cervical canal one of the most important points that must be observed is that the canal should be thoroughly cleansed and dried in order that the medication may come into actual contact with the infecting organisms which lie in the cervical glands. It is utterly impossible for any drug to accomplish this in the presence of a thick discharge, or even the usual cervical plug of mucus, which effectively protects the underlying organisms from the action of any antiseptic. Therefore, in order to get the best results, it has been our practice to expose the cervix by means of a bivalve speculum, wipe away the major portion of the discharge and then thoroughly spray the cervix with an alkaline solution, in order to dissolve the mucus. The cervix is again dried and then an applicator soaked in an alkaline solution (liquor antisepticus alkalinus) is passed into the canal as far as the internal os and moved to and fro, after which a dry cotton swab is passed into the canal and the thin discharge removed. This process is repeated several times until all of the mucus is removed and the canal is left clean and dry. We are then ready to apply our medication, which may be any one of the usual gonococccides. Our own preference is for a 10 or 12.5 per cent. solution of silver nitrate, which is vigorously applied to the canal

as far as the internal os, and immediately afterward tincture of iodine is similarly applied. These two drugs form a fresh silver iodide in the cervical canal, as can be seen by the characteristic yellow color that is produced. Not infrequently the patient will complain of some lower abdominal cramps as soon as the tincture of iodine is applied. This is merely a uterine colic, due to the stimulation of the muscle produced by the iodine fumes, and need cause no alarm, as it will disappear in a minute or two. Following this application the cervix and cul-de-sac are thoroughly dried and the speculum withdrawn. Only in very exceptional cases is a tampon inserted.

The patient continues her douches at home and reports to the office for treatment two or three times a week for the first three weeks, after which time the condition is usually so improved that douches can be discontinued and the interval between treatments can be lengthened. When the discharge has lost all of its purulent character and has become scanty, smears should be taken, and after three negative smears, one of which should be taken just after a menstrual period, the patient may be discharged.

Such is the technic that has given us more than satisfactory results, but it is only by a careful observance of details that results will be obtained, and at times the successful execution of a treatment is a trying ordeal for the physician. Any practitioner who would undertake to treat these cases should bear in mind two important points: In the first place, any particular treatment takes time, especially in the beginning of the disease, when the discharge is profuse and it is practically impossible to follow this technic closely in less time than fifteen minutes, which is more time than many practitioners are accustomed to spend upon these cases. In the second place the treatment should be as free from pain as possible, because if the patient is not comfortable she will not remain quiet upon the table, it will be impossible to get good exposure of the parts, and without good exposure the treatment cannot be properly administered. This point is also of special importance in the beginning of the disease, when the vulva is so tender as a result of the irritating discharge that the slightest pressure causes pain, while the insertion of a speculum seems to be out of the question. In these cases I do not hesitate to use a local anesthetic, which is applied on a pledget of cotton to the vaginal outlet. By this means, together with a little encouragement to the patient, I have never had to abandon a treatment on account of pain; indeed, I have been successful in introducing a speculum in several cases after futile as well as painful attempts have been made by colleagues.

As was stated in the beginning of this paper, nothing new is presented in the field of therapeutics, but if the practitioner will follow the technic above outlined and follow it in detail, I feel sure that he will be rewarded by results that will change his opinion relative to the gloomy prognosis of this disease.

A STUDY OF SUGAR MOBILIZATION BASED UPON 228 HUMAN CASES.¹

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THE advent of microchemical methods in blood chemistry has opened many new fields for investigation, one of these being the metabolism of sugar. Our present knowledge of sugar metabolism, based solely upon chemical examination of the blood, may be summarized in a brief statement: The normal sugar content of the blood varies between 60 and 120 mg. per 100 c.c.,² and when the concentration of blood sugar rises above 180 mg. per 100 c.c. then sugar usually appears in the urine.³

Jacobsen,⁴ who determined the amount of blood sugar present before and at different periods after the administration of relatively large amounts of glucose, found that after the administration of glucose there was a sharp rise in the percentage of blood sugar, which attained its maximum in about one hour and then slowly receded, returning to normal within two hours after the ingestion of the sugar. Other investigators,⁵ by employing slight modifications of Jacobsen's method, have arrived at similar conclusions.

The results of these investigations of sugar tolerance, as they are called, have usually been presented in the form of a curve. These curves have been plotted for varying time intervals; thus, some observers, have examined the blood every fifteen minutes, while others, in order to determine the duration of the reaction, have continued observation for four, five and six hours.

In the present investigation, metabolism of sugar has been viewed as a functional test and not as a study of metabolism. This attitude having been adopted, rigid standards must be laid down for the technic of the test itself and for the manner in which the resulting

¹ The clinical observations recorded in this paper were made in greater part at the Lenox Hill Hospital and the Lincoln Hospital. Through the courtesy of Drs. Semken, Jessup, Fitch and Grant, forty-six cases were examined by them in the wards and in the laboratory of the New York Skin and Cancer Hospital. Their results were kindly given us for inclusion in this paper. We beg to express our thanks and appreciation to them and to those others who have so generously provided us with clinical material.

² Williams and Humphreys: *Arch. Int. Med.*, 1919, xxiii, 537.

³ Hamman and Hirschman: *Arch. Int. Med.*, 1917, xx, 761.

⁴ *Biochem. Ztschr.*, 1913, lvi, 471.

⁵ Hopkins: *AM. JOUR. MED. SC.*, 1915, cxlix, 254. Taylor and Hutton, Jr.: *Biol. Chem.*, 1916, xxv, 173. Janney and Isaacson: *Arch. Int. Med.*, 1918, xxii, 160.

data are presented. A functional test presupposes that under the influence of a given definite stimulus the organism in a definite time period reacts in a definite manner. All extrinsic conditions must be constant, so that all variations can definitely be ascribed to differences in the individual.

The technic of the test as applied to patients in the wards of the various hospitals was as follows: After an all-night fast the individual was given 100 gm. of anhydrous glucose dissolved in 300 c.c. of weak tea. Both blood and urinary specimens were obtained just before giving the glucose and again 45 and 120 minutes thereafter. The chemical examinations of the blood were made after the Meyers-Bailey⁶ modification of the Lewis-Benedict⁷ method. The urinary specimens were examined according to the quantitative method described by Benedict.

We are aware that curves constructed on sugar values obtained at different time intervals than those chosen, would more accurately establish the point of maximum sugar concentration in the blood and that our method of glucose administration may be open to dispute. However, the point of maximum sugar concentration is not of importance from our standpoint, and varying the amount of glucose given according to the body weight (method of Janney and Isaacson), alters the burden placed on the organism. Variations of this character are not made in other functional tests. Thus with phenolsulphonephthalein the amount of dye injected is not changed to conform to the age, weight or other condition of the individual to be tested.

The investigations recorded in the succeeding paragraphs were prompted by the results recorded in another publication.⁸ It was distinctly stated in that report that it was a preliminary one and it was emphasized that no definite conclusions were drawn. Our results as incorporated in that article, using the time intervals as given in this paper, seemed to indicate, on the basis of the material available, that there was a type of reaction peculiar to cancer.

The data collected as a result of the examinations recorded here will be considered under two heads: (a) statistical, and (b) pathological condition present.

Following the method outlined, three different types of reaction were encountered. The three types closely follow those described by McCasky.⁹ In the type arbitrarily termed 1 the blood sugar at the 45 minute interval rises above the zero hour figure, and at the 120 minute interval is as high as or higher than at the 45 minute interval. In the type classed as 2 the rise at the 45 minute interval occurs as in type 1, but at the 120 minute interval the amount of

⁶ Jour. Biol. Chem., 1916, xxiv, 147.

⁷ Ibid., 1915, xx, 61.

⁸ Rohdenburg, Bernhard and Krehbiel: Jour. Am. Med. Assn., 1919, lxxii, 1528.

⁹ Jour. Am. Med. Assn., 1919, lxxiii, 245.

blood sugar has fallen more or less completely to the original figure. In the last type called 3 the initial sugar concentration is higher than or the same as that at 45 minutes, and the 120 minute interval shows a return to the original figures more or less complete, sometimes even going much higher.

If the pathological condition be completely disregarded and the cases be grouped solely according to the type of reaction found some interesting facts are demonstrable. The first 166 cases examined have been considered purely from this standpoint.

TABLE I.

	Type 1.	Type 2.	Type 3.
No sugar in urine . . .	33 (50%)	49 (53%)	8 (100%)
Sugar in urine . . .	33 (50%)	43 (47%)	0
Total	66 (39%)	92 (55%)	8 (6%)

RENAL THRESHOLD OF THOSE SHOWING SUGAR.

		Mg. per 100 c.c.		Mg. per 100 c.c.		Mg. per 100 c.c.	
		Type 1.	Number.*	Type 2.	Number.*	Type 3.	Number.*
Zero	High	212	4	212	1		
	Average	170	13%	212	4%	0	
	Low	126	..	212	..		
45 mins.	High	304	16	400	30		
	Average	209	48%	188	69%	0	
	Low	135	..	141	..		
120 mins.	High	360	13	264	12		
	Average	226	39%	186	27%	0	
	Low	153	..	55	..		
NOT SHOWING SUGAR.							
Zero	High	198	..	138	..	212	
	Average	153	..	126	..	142	
	Low	45	..	55	..	106	
45 mins.	High	265	..	280	..	192	
	Average	202	..	178	..	119	
	Low	72	..	100	..	83	
120 mins.	High	330	..	220	..	141	
	Average	292	..	139	..	60	
	Low	126	..	62	..	60	

* Indicates number of cases showing sugar in urine at this time interval.

The three types were represented (Table I) in the following proportions: type 1, 39 per cent.; type 2, 55 per cent.; type 3, 6 per cent. If each type in turn be considered from the standpoint of sugar elimination in the urine it will be noted that 50 per cent. of type 1 showed sugar at some period during the test as compared with 47 per cent. of type 2 and none of type 3. If each type be divided according to the excretion of sugar in the urine and the average concentration of blood sugar be compared in those excreting sugar and those not, it will be noted that the elimination of sugar

apparently bears but a slight relation to the concentration in the blood. Thus in type 1 in those showing sugar in the urine the average concentration of blood sugar at the various time periods was 170, 209, 226 mg., while in the same group those not showing sugar in the urine had as averages for the same periods 153, 202, 292 mg. In type 2 the figures for those showing sugar in the urine were 212, 188, 186 mg., while those showing no sugar had as averages 126, 178, 139 mg. Type 3 showed no sugar in the urine. In type 1, therefore, the average sugar concentration at the end of 120 minutes was higher in those showing no sugar in the urine than in those showing sugar, and this average was higher than the commonly accepted concentration of a normal renal threshold (180 mg.). Type 2, on the other hand, the figures for the zero hour being disregarded, since but one case showed sugar at that period, follows the commonly accepted standard. There is evidently some factor other than the mere concentration of sugar in the blood stream, which is responsible for the glycosuria.

The criticism may perhaps be made that because of the time intervals chosen the point of maximum sugar concentration in the blood was not ascertained; hence our deductions are faulty. If this criticism be true it applies with equal force to all groups and it does not explain why with one group of type 1 sugar should appear in the urine, with a concentration in the blood stream averaging 62 mg., less than in another group of the same type which did not excrete sugar.

The wide variation between maximum and minimum in any given group at any time interval would indicate that the actual determination of a point of maximum sugar concentration can have but little value in the diagnosis of pathological conditions, whatever may be its value from a metabolic standpoint. Varied as were the pathological conditions considered in our experiments it is interesting to note that in many of them the figures for the zero hour were distinctly higher than those currently accepted as normal.

An analysis correlated with the diagnosis of the patients examined is fully as interesting as the purely statistical review just made. In 228 cases reported here the diagnosis of all but 13 has either been confirmed by the pathological report (culture, section, or autopsy) or by the subsequent course of the case. The various pathological conditions encountered have been grouped, the reactions classified and the average figures given in Table II, while in Table III the data for each case are given individually.

In nephritis our results in agreement with those recorded by others show an initial hyperglycemia, with 75 per cent. of the cases giving a type 2 reaction.

In the two conditions pathologically classed as granulomata, in which the exciting cause is known—tuberculosis and syphilis—an initial hyperglycemia is not present, and while 60 per cent. of the

tuberculous cases show type 1 reaction, 72 per cent. of the syphilitics showed type 2. It is interesting to note that though the concentration of blood sugar was lower in tuberculosis than in syphilis, nevertheless a larger percentage of tuberculous cases excreted sugar. If concentration of the blood sugar were the only factor concerned in the excretion of sugar then the reverse should have occurred.

TABLE II.

Pathological condition.	No. of cases.	Mg. sugar per 100 c.c. blood.			Per cent. showing sugar in urine.	Per cent. of total number in this group.
		0 hr.	45 min.	120 min.		
TYPE I.						
Nephritis	2	170	233	294	50	25
Tuberculosis	4	97	156	198	50	60
Syphilis	2	77	178	205	0	28
Diabetes	4	139	310	390	100	37
Thrombo-angiitis obliterans	8	114	184	225	62	22
Pregnancy	2	141	169	188	50	66
Chorea	2	129	177	236	0	50
Exophthalmic goitre	2	123	211	238	100	50
Simple goitre	1	86	204	250	100	100
Pyogenic infections	3	119	165	169	0	30
Degenerative conditions	2	96	163	239	0	50
Benign tumors	4	136	204	252	50	31
Epithelioma	17	106	158	198	76	56
Carcinoma, stomach	11	111	191	219	27	61
Carcinoma, intestines	4	105	172	193	50	50
Carcinoma, breast	4	95	183	196	25	30
Carcinoma, genital organs	1	110	250	360	100	20
Malignant tumors not classified	10	111	192	225	30	66
TYPE 2.						
Nephritis	6	131	217	153	50	75
Tuberculosis	3	91	188	100	38	30
Syphilis	5	97	177	120	20	72
Diabetes	5	162	319	269	100	63
Thrombo-angiitis obliterans	34	119	191	154	41	75
Pregnancy	1	126	204	152	100	33
Chorea	2	121	240	189	0	50
Exophthalmic goitre	2	105	122	118	50	50
Pyogenic infections	7	101	174	152	14	70
Degenerative conditions	2	97	160	114	50	50
Benign tumors	6	113	202	143	66	46
Epithelioma	13	95	174	126	46	44
Carcinoma, stomach	6	102	220	184	50	33
Carcinoma, intestines	4	137	233	162	25	50
Carcinoma, breast	8	111	186	144	37	61
Carcinoma, genital organs	4	125	208	156	0	80
Malignant tumors not classified	3	109	170	135	0	20
TYPE 3.						
Tuberculosis	1	125	83	66	0	10
Thrombo-angiitis obliterans	1	106	106	106	0	3
Benign tumors	3	136	115	99	0	23
Carcinoma, stomach	2	118	105	156	50	6
Carcinoma, breast	1	117	100	95	0	9
Malignant tumors not classified	2	144	122	119	50	13

TABLE III.

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
16697	Tuberculosis	105	213	266	+	+	+
16762	"	100	107	111	+	-	-
L 79	"	100	200	260	-	-	-
L 89	"	112	210	50	-	-	-
L 460	"	45	72	157	-	+	-
487	"	125	83	66	-	-	-
1356	"	106	180	204	-	-	-
3836	"	72	204	114	-	-	-
4283	"	90	150	138	-	-	-
2726	"	128	168	192	-	-	-
4634	Syphilis	144	189	144	-	-	-
4239	"	117	245	147	-	-	-
1858	"	92	232	268	-	-	-
1337	"	96	232	180	-	-	-
L 86	"	65	115	75	-	-	-
440	"	66	105	55	-	-	-
J O B	"	62	125	142	-	-	-
P 502	Pregnancy	126	204	152	-	+	+
5708	"	136	156	186	+	+	+
3980	"	146	183	189	-	-	-
D 1210	Diabetes	144	312	304	-	+	+
2878	"	186	268	288	-	+	+
801	"	172	315	260	+	+	+
P 610	"	212	380	310	-	+	+
P 304	"	150	280	384	+	+	+
P 508	"	204	400	384	+	+	+
P 608	"	80	192	90	+	+	+
4046	"	81	384	500	-	+	+
D 210	Exophthalmic goitre	106	141	110	-	+	-
5809	"	126	232	264	-	-	+
6570	"	104	104	126	-	-	-
P 820	"	120	190	212	-	+	+
1784	Simple goitre	86	204	250	-	-	+
3839	Chorea	122	208	232	-	-	-
3840	"	136	147	240	-	-	-
4242	"	114	216	138	-	-	-
4243	"	129	265	240	-	-	-
L 76	Nephritis	120	200	180	-	-	-
77	"	100	116	104	-	-	-
80	"	200	340	100	-	-	-
87	"	154	200	166	-	-	-
P 1	"	96	244	212	-	-	-
D 279	"	117	204	156	-	-	+
4363	"	168	265	348	+	+	+
2735	"	172	212	240	-	-	-
2916	Cholecystitis	135	144	144	-	-	-
3205	Fistula in ano	105	168	180	-	-	-
2633	Rheumatic fever	80	219	177	-	-	-
P 795	Endocarditis	118	184	189	-	-	-
4632	"	120	200	188	-	-	-
4401	Suppurative arthritis	126	189	184	-	+	+
3002	"	96	138	126	-	-	-
2576	Lung abscess	106	190	188	-	-	-
16682	Cellulitis, neck	85	100	76	-	-	-
16662	Abscess, face	95	187	129	-	-	-
2349	Postoperative adhesions	96	192	165	-	-	-
1286	Chronic appendicitis	106	212	192	-	-	-

TABLE III—continued.

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
3138	Chronic appendicitis	117	240	285	—	—	+
P 145	Acromegaly	126	144	129	—	—	—
2585	Cretinism	126	132	82	—	—	—
D 286	Spondylitis	82	235	265	—	+	+
2562	Bronchial asthma	144	172	201	—	—	—
L 74	Cirrhosis of liver	100	200	320	—	—	—
L 83	"	71	100	75	—	—	+
L 78	Apoplexy	124	220	154	—	—	—
3851	Myocarditis	92	126	159	—	—	—
S 1	Normal male	112	159	130	—	—	—
4447	Leukemia	159	204	160	—	—	—
129	Tobacco-poisoning	120	330	219	—	+	+
16724	Cystitis mastitis	175	266	210	—	+	—
D 358	Exostosis	78	152	111	—	—	—
D 186	"	147	228	131	—	+	+
3598	Fibromyoma uteri	212	322	336	—	+	+
408	"	68	71	142	—	—	—
16640	"	86	63	74	—	—	—
D 184	Foreign body	116	228	106	—	—	—
D 481	"	57	95	76	—	—	+
P 146	Cyst adenoma of ovary	156	120	84	—	—	—
2066	"	198	265	320	—	—	—
453	Chronic inflammation	76	157	213	—	+	+
1304	Papilloma of bladder	106	245	225	—	—	+
2483	Congenital cystic kidney	168	164	141	—	—	—
16589	Epithelioma of penis	100	175	142	+	+	+
16620	" skin	86	199	249	+	+	+
16644	" cheek	100	117	175	—	+	+
16643	" lip	117	187	199	—	+	+
16440	" lip	153	229	260	—	+	+
16339	" cheek	133	166	133	—	—	+
16445	" larynx	142	142	229	—	—	+
16635	" larynx	117	213	175	+	+	+
16675	" lip	95	95	100	—	+	+
16744	" penis	100	160	214	—	—	—
16599	" lip	101	125	142	—	+	—
4245	" tongue	150	159	162	—	—	—
D 129	" buttock	166	236	180	—	—	+
3045	" larynx	129	192	192	—	+	+
z 16339	" cheek	64	187	105	—	—	—
z 16435	" face	99	142	153	—	—	+
H. S.	" lip	86	142	199	—	+	—
z 16378	" lip	105	160	125	—	—	—
1834	" cheek	122	228	144	—	—	—
2068	" cheek	80	244	265	—	—	—
1589	" esophagus	82	160	220	—	—	—
1691	" cheek	106	174	144	—	—	—
16357	" tongue	55	178	154	—	—	—
16450	" mouth	105	175	222	—	—	+
16439	" cheek	111	135	229	—	+	+
16368	" neck	100	166	105	—	+	+
16390	" nose	76	86	153	—	—	+
16436	" mouth	54	160	100	—	+	+
16404	" eyelid	55	122	62	—	—	+
16272	" face	57	100	62	—	—	—
2834	Carcinoma of stomach	116	168	230	—	—	—
2939	"	78	215	210	—	—	—

TABLE III—*continued*.

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
1621	Carcinoma of stomach	106	275	245	—	—	+
2019	" "	110	183	183	—	—	+
2415	" "	76	212	212	—	—	—
859	" "	120	144	232	—	—	—
712	" "	108	228	288	—	+	+
974	" "	106	100	192	—	—	+
L 82	" "	100	240	220	—	+	+
L 90	" "	130	110	120	—	—	—
4648	" "	145	190	190	—	—	—
4174	" "	138	208	112	—	—	—
2429	" "	136	304	304	—	—	—
2096	" "	98	160	126	—	+	+
2708	" "	132	190	200	—	—	—
2794	" "	102	138	168	—	—	—
2946	" "	96	224	190	—	—	—
3353	" "	74	188	224	—	+	+
3728	" "	110	165	196	—	—	—
4079	" colon	120	240	156	—	—	+
4362	" colon	108	212	159	—	—	—
4352	" colon	174	265	185	—	—	—
S 16415	" cecum	116	200	216	—	+	—
1277	" sigmoid	55	129	157	—	—	+
7305	" rectum	123	158	189	—	—	—
2687	" rectum	126	205	240	—	—	—
D 718	" rectum	156	215	148	—	—	—
2001	" liver	123	189	184	—	—	—
4208	Hypernephroma of liver	126	212	212	—	—	+
2119	Carcinoma of pancreas	120	160	210	—	—	—
551	" pancreas	212	192	138	—	—	—
985	" pancreas	114	240	272	—	—	—
1895	" breast	86	232	236	—	+	+
P 2	" breast	138	183	117	—	—	—
P 3	" breast	126	162	150	—	+	+
2408	" breast	126	240	192	—	—	+
1456	" breast	96	180	180	—	—	—
L 75	" breast	100	250	170	—	—	—
L 84	" breast	144	180	150	—	—	—
L 85	" breast	100	166	120	—	—	—
L 88	" breast	80	146	114	—	—	—
S 16455	" breast	76	160	110	—	+	+
16406	" breast	117	100	95	—	—	—
2988	" breast	90	152	192	—	—	—
D 111	" breast	110	168	176	—	—	—
1979	" ovary	135	204	132	—	—	—
2512	Sarcoma of uterus	106	174	110	—	—	—
1043	Carcinoma of uterus	138	174	164	—	—	—
L 81	" uterus	120	280	220	—	—	—
S 16451	" uterus	110	250	360	—	—	+
L 98	Sarcoma of femur	98	170	220	—	—	—
2050	" kidney	90	132	76	—	—	—
16404	" orbit	101	187	199	—	—	+
2411	Carcinoma of lung	106	150	192	—	—	—
P 4	" lung	100	165	230	—	—	—
3056	" bladder	138	240	290	—	—	+
1436	" bladder	116	189	146	—	—	—
16673	" tonsil	76	63	100	—	+	+
16739	Metastatic carcinoma	120	199	213	—	+	+
5810	" "	96	204	215	—	—	—

TABLE III—continued.

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
W M 1	Thrombo-angiitis obliterans	106	138	216	—	—	+
2	"	108	280	198	—	—	—
3	"	168	192	126	—	—	+
4	"	116	192	168	—	—	—
5	"	106	116	96	—	—	—
6	"	142	344	288	—	—	+
7	"	210	300	280	—	+	+
8	"	112	200	230	—	—	—
9	"	124	180	159	—	—	—
10	"	100	144	126	—	—	—
11	"	96	159	116	—	—	—
12	"	136	144	96	—	+	+
13	"	129	265	240	—	—	+
14	"	96	108	104	—	—	—
15	"	126	164	96	—	—	—
16	"	99	138	116	—	—	—
17	"	116	184	174	—	—	—
18	"	129	200	174	—	+	+
19	"	116	162	129	—	+	—
20	"	114	132	144	—	—	—
21	"	100	162	120	—	+	—
22	"	126	150	116	—	—	—
23	"	120	129	106	—	—	—
24	"	106	106	106	—	—	—
25	"	96	320	192	—	+	+
26	"	100	174	138	—	+	—
27	"	116	159	116	—	—	—
28	"	116	189	174	—	—	—
29	"	102	198	198	—	—	—
30	"	110	189	120	—	+	+
31	"	106	189	159	—	—	—
32	"	110	212	96	—	+	—
33	"	100	174	100	—	—	—
34	"	120	153	112	—	—	—
35	"	116	150	190	—	—	—
36	"	106	138	216	—	+	+
37	"	108	280	198	—	+	—
38	"	96	159	112	—	—	—
39	"	153	240	208	—	+	—
40	"	114	212	176	—	—	—
41	"	156	252	350	—	+	+
42	"	106	114	106	—	—	—
D 174	"	100	265	280	—	+	+
DIAGNOSIS OF FOLLOWING		NOT	PROVED				
D 42	Carcinoma of lung	100	208	196	—	—	—
2172	Brain tumor	176	240	264	—	—	+
1306	Ulcer of stomach	86	184	232	—	+	+
1390	" stomach	86	174	183	—	—	+
1624	Carcinoma of stomach	116	180	230	—	—	—
1603	" stomach	78	240	210	—	—	—
1674	" stomach	120	240	156	—	—	—
L 73	" stomach	120	200	160	—	—	—
2308	Gastroptosis	120	150	86	—	+	+
3055	"	156	176	168	—	—	+
7868	Neurasthenia	126	106	60	—	—	—
4369	"	96	114	123	—	—	—
861	Severe secondary anemia	108	152	144	—	—	—

The diabetics examined showed, as was to be expected, an initial hyperglycemia, with 60 per cent. of the cases giving a type 2 curve.

In the cases of thrombo-angiitis the initial figures were practically normal and the type of reaction in 75 per cent. of the cases was that of type 2.

In pregnancy there is also an initial hyperglycemia, and 66 per cent of the cases gave a type 1 reaction. Pyogenic infections gave 70 per cent. type 2 reaction.

In degenerative tissue conditions, such as cirrhosis of the liver, myocarditis, etc., one case was observed with a blood sugar concentration of 239 mg. without urinary leakage.

As we have stated before, our original paper had to do with the reaction in cases of cancer. Our present report necessitates a very considerable modification of our previous statements. In that paper we considered what we have since termed type 1 to be a possibly specific reaction in cancer.

In our series of benign tumors we have found 31 per cent. to give type 1 reaction as compared with 56 per cent. of epitheliomata, 61 per cent. of gastric carcinomata, 50 per cent. of intestinal carcinomata, 30 per cent. of breast carcinomata, 20 per cent. of genital organ carcinomata and 66 per cent. of other non-grouped malignant tumors. The actual number of cases is given in Table III. Initial hyperglycemia occurs in some instances, but is not constant. The fact that so high a percentage of type 1 reaction occurred with epitheliomata not showing cachexia renders untenable the theory that the high percentage given by gastric carcinomata is due to cachexia and the demand of the tissues for sugar.

CONCLUSIONS. It is evident, from the data here presented, that the organism may respond in one of three ways after the ingestion of 100 gm. of glucose. Neither of these three reaction types can be considered as diagnostic of any given pathological condition, though, in general, conditions associated with increased growth energy show a higher percentage of type 1 reaction. There is no fixed type of reaction even in metabolic disturbances, absolutely similar curves being found in conditions as widely different as diabetes, tuberculosis, epithelioma and pregnancy. Many diseased conditions are accompanied by hyperglycemia. The concentration of blood sugar is not the sole factor concerned in the development of glycosuria.

THE GERMICIDAL VALUE OF POTASSIUM MERCURIC IODIDE.

BY DOUGLAS MACFARLAN, M.D.,

SINCE the second year of the war the subject of antiseptics has acquired a new interest and need has arisen to refresh and revise

our knowledge of the relative merits and faults of various germicides. In former times personal preferences, based largely on empiricism, led to the choice of this or that chemical substance for the purpose of disinfecting operative sites and wounds. Oftentimes certain collateral qualities of the germicides, such as solubility, reputed lack of toxicity and so forth, rather than their actual killing power on bacteria under surgical conditions, were emphasized.

Any comparison of germicides should be based (1) on their bactericidal efficiency and (2) on their physical and chemical properties. For some time past the writer, realizing the disadvantages of many of the germicides in general use, has devoted himself to the study of potassium mercuric iodide.

Earlier experiments already reported¹ have demonstrated several marked advantages of this substance over other iodine and mercury salts in addition to its value in the treatment of infectious conditions,^{2 3 4}. Watson⁵ and Hinman⁶ obtained fresh evidence of its high germicidal potency, while Rosenberger,⁷ working with an analogous compound, confirmed the efficiency of this type of mercury salt.

Potassium mercuric iodide is a distinct chemical entity, formed by the direct combination of two molecules of potassium iodide with one molecule of mercuric iodide, and has the formula K_2HgI_4 or $HgI_2 \cdot 2KI$. For this reaction, and also in order that the subsequent conversion of this double salt into the red iodide of mercury may be prevented, an excess of potassium iodide is necessary. In the crystalline state the salt is deliquescent, and upon taking up water, readily deposits the red mercuric iodide. It may, however, be obtained in tablet form, in which the two salts (mercuric iodide and potassium iodide) are bound by an inert soluble excipient and readily yield clear, stable solutions of the double salt. This is by far the most convenient form in which to obtain and employ this substance.

Before considering the high germicidal potency of potassium mercuric iodide four distinctive and valuable features making for its superiority over other salts of mercury and iodine may well be considered.

¹ Macfarlan, Douglas: Notes in the Study of Potassium Mercuric Iodide, *Jour. Am. Med. Assn.*, January 3, 1914, lxii, 17-19.

² Macfarlan, Douglas: Still Another Suggestion for Atrophic Rhinitis; the Double Iodide of Mercury and Potassium, *Jour. Ophth., Otol. and Laryng.*, October, 1913, vol. xix.

³ Macfarlan, Douglas: A Rationale of a New Treatment for the Acute Frontal Sinusitis, *Jour. Ophth., Otol. and Laryng.*, September, 1915, vol. xxi.

⁴ Macfarlan, Douglas: A Consideration of Pyorrhoea and the Rationale of a New Remedy, with Case Reports, *Jour. Ophth., Otol. and Laryng.*, November, 1916, vol. xxii.

⁵ An Improved Substitute for Iodized Catgut Sutures, *Surg., Gynec. and Obst.*, January, 1916, xxii, 114-115.

⁶ Urinary Antiseptics, *Jour. Am. Med. Assn.*, November 20, 1915, lxxv, 1769.

⁷ On Lithio Mercuric Iodide, *Am. Med.*, June 25, 1904, vii, 1021.

1. *Solubility.* It is readily soluble in both water and alcohol as well as in acetone.

2. *Toxicity.* As compared with the most prominent metallic germicide—mercuric chloride—it is far less toxic, and, in dilutions effective for germicidal use, the factor of safety renders it comparatively harmless for irrigations of mucous membranes or for any purpose in which there is a likelihood of its being swallowed. Even a 1 per cent. solution may be taken internally in doses of six to eight drops without producing gastric irritability, while one would have to swallow about 30 c.c. of the 1 to 1000 solution or 300 c.c. of the 1 to 10,000 solution to obtain the maximum medicinal dose.

3. *Lack of Irritation.* One-half of 1 per cent. solutions are slightly irritating to the mucous membranes, causing a burning sensation with the stimulation of a watery secretion. Solutions of these strengths have little or no irritating effect on the skin when applied for twenty-four hours by a wet pack or compress, while dilutions of 1 to 1000 or more cause none of the disagreeable effects upon the hands produced by similar solutions of bichloride of mercury.

4. *Non-precipitation of Proteins.* Contrary to the action of other metallic germicides in the presence of proteins, potassium mercuric iodide fails to precipitate these substances. Experiments by the author have shown that so soluble is this salt in protein solutions that human blood serum readily dissolves 100 per cent. of potassium mercuric iodide without any appreciable coagulation or precipitation of the serum albumin or globulins. This lack of affinity for serum proteins is an important factor in those cases in which it is desired to achieve potent germicidal action in the presence of blood, pus or other tissues. That the germicidal action of the double salt, unlike other antiseptics and germicides, is only slightly diminished by the presence of organic matter will be shown in Table VII.

GERMICIDAL ACTION. Potassium mercuric iodide has long been known as a potent germicide, exerting not only an antiseptic but a true killing power in high dilutions. In the well-known table of Park⁸ the red iodide of mercury, the active component of the double salt, stands at the head of the list for potency. Earlier experiments by the author, reported in 1914,¹ showed that potassium mercuric iodide in a dilution of 1 to 80,000 killed such organisms as *Bacillus typhosus*, *Staphylococcus aureus*, *Bacillus bulgaricus*, *Bacillus acidi lactici* and a yeast after a twenty-four-hour exposure, while Watson,⁵ comparing the action of the double iodide with that of iodine solutions, found that the former was far superior in its killing action on *Staphylococci*, *Bacillus coli* and even the sporulating *Bacillus subtilis*.

With a view to gaining additional and more exact information concerning the germicidal action of potassium mercuric iodide the

⁸ Pathogenic Microorganisms, 6th ed., Philadelphia, Lea & Febiger, 1917, p. 668.

TABLE IV.—BACILLUS COLI COMMUNIS (CONTINUED).

Dilution: K ₂ HgI ₄	Time of exposure (hours).								
	$\frac{1}{2}$	1	2	3	4	5	6	12	24
1-100,000	X	X	X	X	X	X	X	X	X
1- 90,000	X	X	X	X	X	X	X	X	0
1- 80,000	X	X	X	X	X	X	X	X	0
1- 70,000	X	X	X	X	X	X	X	X	0
1- 60,000	X	X	X	X	X	X	X	X	0
1- 50,000	X	X	X	X	X	X	X	X	0
1- 40,000	X	X	X	X	X	X	X	0	0
1- 30,000	X	X	X	X	X	X	0	0	0
1- 20,000	X	X	X	0	0	0	0	0	0
1- 10,000	X	X	0	0	0	0	0	0	0
1- 5,000	X	0	0	0	0	0	0	0	0
1- 1,000	0	0	0	0	0	0	0	0	0
Broth control	X	X	X	X	X	X	X	X	X

TABLE V.—BACILLUS SUBTILIS.

Dilution: K ₂ HgI ₄	Time of exposure (minutes).							
	3	5	10	20	30	40	50	60
1-5000	X	X	X	X	X	X	X	X
	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
1-4000	X	X	X	X	X	X	X	X
1-3000	X	X	X	X	X	X	X	X
1-2000	X	X	X	X	X	X	X	X
1-1000	X	X	X	X	X	X	X	X
	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
1- 500	X	X	X	X	X	X	X	0
	(X)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
1- 100	X	0	0	0	0	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Broth control	X	X	X	X	X	X	X	X
X = Growth	} 1st series.							
0 = No growth								
(X) = Growth	} 2d series.							
(0) = No growth								

TABLE VI.—BACILLUS SUBTILIS (CONTINUED).

Dilution: K ₂ HgI ₄	Time of exposure (hours)						
	$\frac{1}{2}$	1	2	3	6	12	24
1-100,000	X	X	X	X	X	X	X
1- 90,000	X
1- 80,000	X
1- 70,000	X
1- 60,000	X
1- 50,000	X	X	X	X	X	X	X
1- 40,000	X	X	X	X	X	X	X
1- 30,000	X	X	X	X	X	X	X
1- 20,000	X	X	X	X	X	X	X
1- 10,000	X	X	X	X	X	X	0
	(X)	(X)	(X)
1- 5,000	X	X	X	X	X	0	0
	(X)	(X)	(X)
1- 1,000	X	X	X	X	0	0	0
	(X)	(X)
Broth control	X	X	X	X	X	X	X

The above tables are self-explanatory. The results prove that potassium mercuric iodide possesses a remarkably high germicidal

efficiency. The fact that a pus-producing organism such as the Staphylococcus is killed in five minutes by a 1 to 5000 solution shows that this double iodide may be effectively used in dilutions which are incapable of producing irritation to the most sensitive tissues or of causing poisoning under the usual therapeutic conditions. In Tables V and VI the rapid action of 1 to 100 and even to 500 solutions on a sporulating culture of Bacillus subtilis may be taken as an indication of the action of this double salt on pathogenic sporulating bacilli such as the organisms of tetanus, anthrax, gas gangrene and malignant edema.

In order to determine to what extent the presence of organic matter, serum proteins especially, might interfere with or diminish the bactericidal action of potassium mercuric iodide, the following experiment was carried out:

I. *Technic.* To tubes containing 2 c.c. of the different dilutions of the germicide was added sufficient human serum to give an actual coagulable protein content of 0.5 per cent. (determined by gravimetric method). The solution remained perfectly clear, but solidified on boiling. The tubes were allowed to stand twenty-four hours to allow any possible reaction between the double iodide and the albumin to take place. The tubes were then inoculated with 0.1 c.c. of an actively growing broth culture of Staphylococcus albus freshly isolated from a human infection. After the stated period of exposure, subcultures, using one 2 mm. loopful, were made in liquefied nutrient agar at 40° and then plated. After incubation the plates showed either no growth or a heavy growth, except in the cases of the twelve-hour exposure, where the colonies were few.

II. *Results.*

TABLE VII.

Dilution, K ₂ H ₂ I ₄ .	Staphylococcus, strain A.						Staphylococcus, strain B.						Staphylococcus, strain B, with human serum.									
	Time.						Time.						Time.									
	3"	5"	10"	30"	1'	6'	12'	3"	5"	10"	30"	1'	6'	12'	3"	5"	10"	30"	1'	6'	12'	
1- 500 . . .	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1- 1,000 . . .	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1- 5,000 . . .	X	0	0	0	0	0	0	0	0	0	0	0	0	X	X	X	X	0	0	0	0	0
1- 10,000 . . .	X	X	X	X	0	0	X	X	X	X	X	0	0	X	X	X	X	X	0	0	0	0
1- 50,000 . . .	X	X	X	X	X	0	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
1-100,000 . . .	X	X	X	X	X	0	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

The results show that organic matter in the form of human serum albumin in a concentration of 0.5 per cent. has no appreciable effect on the germicidal action of 1 to 500 and 1 to 1000 solutions of potassium mercuric iodide. As might be expected with the weaker concentration of germicide, protein delays their bacterial action,

but this diminution is relatively slight when compared with McClintic's reports⁹ on the germicidal powers of phenol and some commercial disinfectants in the presence of organic matter.

DISCUSSION. The experiments submitted show that potassium mercuric iodide is a powerful germicide exhibiting marked bactericidal efficiency in high dilutions. Organic matter diminishes its potency to a relatively slight degree. These facts, taken in consideration with its great solubility, its freedom from irritant action and its comparatively low toxicity in the solutions efficacious for germicidal purposes, would seem to recommend this double salt of the iodides of potassium and mercury as the most desirable of the inorganic germicides.

⁹ Hygienic Lab. Bull., April, 1912, lxxxii, 37 *et seq.*

ERRATA.

The Editor assumes responsibility for the unfortunate errors that occurred in the article entitled, "The Oculopupillary Fibers of the Sympathetic System: Division of the First Thoracic Root in Man," by William G. Spiller, M.D., which was published in the issue of this Journal for March, 1920, p. 325. Attention is called to the following corrections:

On page 326, line 39, a comma should be inserted after the word tactile.

On page 331, line 17, "Mmes. Dejerine and Klumpke" should be corrected to read "Madam Dejerine Klumpke."

On the same page, line 41, "She" should be changed to "He."

On line 44 of the same page, "Mmes. Dejerine and Klumpke" should again be corrected to "Madam Dejerine Klumpke."

On page 336, line 21, "her" should be changed to "his," and on line 24 of the same page, "she" should be changed to "he."

REVIEWS

LE TYPHUS EXANTHEMATIQUE. BY D. DANIÉLOPOLU, M.D.,
Professeur Suppléant de Clinique médicale á la Faculté de
Médecine de Bucarest. Médecin de l'hôpital Brancovan. Pp.
512; 87 illustrations and 6 plates in colors and monochrome.
Bucarest: Charles Göbl, 1919.

ONE is accustomed to think of the Balkans as being in a continual state of unrest. From the accounts that we receive from this district we think only of the turmoil and excitement which seems to be continually present there. A good many of us have fixed in our minds the idea that no constructive work is being undertaken there; that the people are more or less existing only on the minimal amount of what in civil life is compatible with keeping body and soul together. Such an impression is distinctly obliterated when one sees a copy of the recent work of Dr. Daniélopolu, which has just come from Bucarest. This book is a splendidly gotten up volume and would do credit to any printer in a country which we consider more enlightened than Roumania. The quality of the paper is good, the printing is clear and without typographical errors, and the illustrations, for the most part, are clear-cut and well reproduced. But the astounding part of the book, at least to the reviewer, is the fact that Dr. Daniélopolu should be able to give the amount of study and work that he has done in this book on typhus fever during all the turbulence of the past war, when conditions were such that it did not seem possible for any physician to do more than the most routine medical work on account of the tremendous demands upon the medical man. The book is largely a volume of original observation, more particularly on the treatment of the disease, and his description of the symptomatology of the fever is a most careful clinical study.

During the war Dr. Daniélopolu had the opportunity to see and study a tremendous number of cases of typhus fever, and it is interesting to know the results of his study of these cases.

In regard to the etiology of the condition, he is didactic in his statement that it is a louse-born disease, and he quotes several reasons why he believes this, all of which are very positive and undoubted.

The louse which transmits the disease is the ordinary body louse, and Dr. Daniélopolu does not believe that the head louse is able to

transmit typhus. The incubation period is supposed to be from five to twenty-one days, but during the course of an epidemic the incubation becomes about equal for all cases, averaging from seven to eight days. Four cases are quoted to prove that the incubation period is of this length of time. For example a nurse on service in the typhus wards wore a special rubber costume; she went to the triage of the hospital without this special rubber costume, was bitten by a louse and seven days after developed the disease. Much the same history is given with three other cases. In the symptomatology of typhus fever the author, in addition to the clear-cut account of the usual symptoms, calls special attention to the unusual changes of the cerebrospinal fluid as made by the study of repeated punctures and which the author insists should be repeated many times on the individual cases. The fluid is of high tension, though never as high as in acute meningitis; it is usually clear, occasionally slightly cloudy and very frequently contains red blood cells, the result of cerebrospinal vasodilation and of effusions in the meninges. Occasionally there is a yellow discoloration which the author was the first to point out and which has been subsequently confirmed by others. Xanthochromia occurs in the cases showing more particularly nervous phenomena. It is necessary to examine the fluid immediately after withdrawal in order to demonstrate this phenomenon. There is also usually an increase in the cellular count of the spinal fluid, and the more severe the case, the higher the number of cells, which are especially increased when there is yellow fluid.

The leukocytes in the blood are much increased, and this increase is usually an absolute increase in all the cellular elements. There are numerous other valuable clinical observations: pulse tracings have been made, eye-ground examinations have been made and complete laboratory studies accomplished, and in every way the cases have been carefully worked up.

The latter part of the book is filled with case reports and details of the author's method of treatment, which consists essentially of the frequent intravenous injections of hypotonic salt solution, the percentage being sixty-five one-hundredths. The results of this treatment have been perfectly astounding. The percentage of the severe cases recovering, according to the special method that the author has of estimating the severity of the disease, varies from 94 to 97 per cent. of those treated by this method, while there is a mortality of from 91 to 100 per cent. in those untreated. J. H. M., Jr.

THE NUTRITION OF THE FETUS. By J. MORRIS SLEMONS, M.D.
Pp. 49. New Haven: Yale University Press, 1919.

In a broad, general way, Dr. Slemons discusses in this monograph the results of the various chemical analyses of the blood of the

mother and fetus made by himself or his assistants during the past few years. We owe much of our present knowledge of the physiology of the placenta and of that fascinating problem, the metabolism of pregnancy, to the careful scientific investigations of the author. One will find here a most readable account of the mechanistic hypothesis of the placental function, the source and mode of transmission of the food of the fetus and the disposal of its waste products.

P. F. W.

THE HEART, PAST AND PRESENT. BY EDGAR LEA, VICT., M. R. C. P. (Lond.), Honorary Physician and Physician-in-Charge, Cardiac Department, Ancoats Hospital, Manchester. Pp. 300. New York: William Wood & Co., 1919.

ACCORDING to the author this volume is in the nature of an inquiry. He has attempted to evaluate, from a study of the past, methods which promise most for future advances in clinical cardiology. He concludes that clinical methods of investigation have been and will be more fruitful than the methods of physiology and pathology.

An elaborate so-called clinico-etiological classification is offered, based not only upon symptoms or physical signs, but the type of cardiac failure in its relation to its exciting cause. Obviously, the attempt to employ such a classification reveals much of the deficiency in our present knowledge, toward which, Dr. Lea believes, intensive clinical inquiry should be directed. To facilitate these studies, he advocates special "heart clinics" in general hospitals, or if found feasible, institutions devoted to cardiac work.

The book reveals the author's enthusiasm for cardiology and his extensive knowledge of the subject. The discussion of heart failure is especially valuable. The point that factors other than mere muscle failure are often most important is stressed. The remarks concerning the relation of acidosis and anoxemia to cardiac disease would better have been omitted; certain of the hypotheses employed already have been rendered dubious.

C. C. W.

HALF A CENTURY OF SMALLPOX AND VACCINATION. BY JOHN C. McVAIL, M.D., LL.D. Pp. 87. Edinburgh: E. and S. Livingstone.

THE volume comprises the Milroy Lectures, delivered by Dr. McVail before the Royal College of Physicians of London on March 13, 18 and 20, 1919, and an Appendix containing a letter from Dr. C. Killick Millard upon this subject.

The book is divided into three main portions. The "natural

division" has been followed, each lecture being given a separate section. The three main headings are as follows: Smallpox as it was and is; vaccination as it was and is; control of smallpox in the present day.

The brochure deals particularly with the subject of smallpox and vaccination in England and Scotland, although references are made to the disease in other countries. Although the efficacy of vaccination does not have to be emphasized, the account of a school epidemic mentioned in the present volume will prove instructive. "An unvaccinated child attended school while suffering from smallpox. In her class were 27 children, of whom (a) 6 had been vaccinated and revaccinated; (b) 13 had been vaccinated only in infancy and (c) 8 were unvaccinated. All those under (a) and (b) escaped attack. All those under (c) were attacked." "In the same room were 42 other scholars, of whom (a) 8 had been vaccinated and revaccinated; (b) 20 had been vaccinated only in infancy and (c) 14 were unvaccinated. All under (a) escaped attack, 5 of those under (b) were attacked, each of them being over eleven years of age, and 12 of the 14 under (c) were attacked."

Emphasis is given that vaccination offers immunity only for a certain period and revaccination at certain fixed periods is necessary. Neither infantile nor revaccination has ever been compulsory on the population of the United Kingdom. Infant vaccination is being more and more neglected. There has been, during the last fifty years, a great diminution in the fatality, the infectivity and the prevalence of smallpox in Great Britain. This diminution has progressed at an increasing rate of speed, particularly during the latter part of the half-century.

One cannot help but being impressed, in reading this interesting exposition on the subject, with the excellence of our vaccination laws.

F. C. K.

QUARTERLY MEDICAL CLINICS. By FRANK SMITHIES, M.D., of the Augustana Hospital, Chicago. April, 1919. Vol. I, No. 2. St. Louis: Medicine and Surgery Publishing Company, Inc.

THE favorable criticism which the first number of *Quarterly Medical Clinics* received at our hands must be repeated in favor of the second number of the first volume. It would be captious, indeed, to call attention to certain omissions, such as, for instance, failure to report the result of blood culture in Case XVI, since the excellence of Dr. Smithies's work is apparent in this volume as in the preceding one. In this as in the first number of the *Quarterly*, cases are presented, laboratory tests detailed, differential diagnoses considered and the presumably correct diagnosis offered, conclusions being arrived at only after careful consideration of all the data at hand.

E. H. G.

DISEASES OF NUTRITION AND INFANT FEEDING. By JOHN LOVETT MORSE, A.M., M.D., Professor of Pediatrics, Harvard Medical School; Visiting Physician at the Children's Hospital; Consulting Physician at the Infants' Hospital and the Floating Hospital, Boston; and FRITZ B. TALBOT, A.M., M.D., Instructor in Pediatrics, Harvard Medical School; Chief of Children's Medical Department, Massachusetts General Hospital; Physician to Children, Charitable Eye and Ear Infirmary; Consulting Physician at the Lying-In Hospital and at the Floating Hospital, Boston. Second edition, revised. Pp. 384. New York: Macmillan Company, 1920.

NOTHING is more important to the student and practitioner of pediatrics than the acquisition of a practical knowledge of the processes underlying digestion and metabolism, so far as these have been accurately determined. It forms the logical introduction to the study of feeding and the clinical disturbances of digestion and nutrition.

In the second edition the authors have incorporated the results of recent research up to April 1, 1918; since that time, until publication, little of importance has been produced. Under the main headings: Physiology and metabolism, breast and artificial feeding, diseases of the gastro-intestinal canal and diseases of nutrition, the whole subject of infant-feeding and nutrition is succinctly and adequately considered. As a result of their extensive clinical and laboratory experience they have been able to adjudicate at times the discordant conclusions of different laboratory workers. Many important decisions as to the various factors in digestion and nutrition, of course, have to be reserved. Not the least valuable feature of the book are the indications afforded as to various lines of profitable research.

J. C. G.

MENTAL DISEASES. A HAND-BOOK DEALING WITH DIAGNOSIS AND CLASSIFICATION. By WALTER VASE GULICH, M.D., Assistant Superintendent, Western State Hospital, Fort Steilacoom, Washington. First edition. Pp. 139; 36 illustrations. St. Louis: C. V. Mosby Company, 1918.

THIS book offers a classification of mental diseases which has been adopted by the American Medico-Psychological Association. Each subject is briefly considered, too brief, in fact, to be of any advantage to the average physician and not sufficiently accurate as to symptomatology, pathology or diagnosis to be of value to the psychiatrist. The facts pertinent to symptoms are not carefully arranged and the fundamental principles are lacking. The book is unscientific and too superficial to be practical.

T. H. W.

SURGICAL CLINICS OF CHICAGO. December, 1919, Vol. III, No. VI.
Pp. 215; 63 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number of the *Clinics*, by reason of containing the index for the volume, is a little reduced in reading matter. It is, however, well up to the standard. Several of the articles are extremely interesting, bearing on some of the most vital questions arising every day in operating. Some clever tricks of technic peculiar to individual operators are described.

This (December) number rounds out the volume for the year, and no surgeon will make a mistake in having the set upon his library shelves.
E. L. F.

DISEASES OF THE STOMACH AND UPPER ALIMENTARY TRACT. By ANTHONY BASSLER, M.D., Professor of Gastro-enterology, New York Polyclinic Medical School and Hospital, etc. Fourth edition. Pp. 120; 881 illustrations and 73 plates. Philadelphia: F. A. Davis Company, 1919.

WE were disappointed in this fourth edition of what we believe to be almost the best of our English books on gastric disorders. The title page promised a revision and enlargement. As for revision, we could find none in the limited time at our disposal; as for enlargement we find the new edition containing no additional pages. About forty-four new lines are devoted to a brief discussion on fractional test-meal examinations and about twenty-five new lines to reversal peristalsis. Both of these topics are timely and interestingly treated. Besides this, four new plates have been added to this edition, showing various normal and abnormal curves obtained by the fractional methods of gastric extraction.

The purchaser of this edition will believe that he has a completely revised work, when such revision has been very scanty. We have long since used this book, and use it much in every-day work. Perhaps it needed no revision or more additions—still, we feel for the doctor and his well-known gullibility. Why not say this work has stood the test of time and the former edition has been exhausted; we are reprinting it with a few additions to cover the recent advances which have been made in this field.

This edition, like its predecessors, treats very exhaustingly of all the common and uncommon conditions which one meets in gastric and upper alimentary diseases. The author has had a wide experience in this specialty, and adds a wealth of personal touch to the text. The illustrations are splendid; many of the roentgen-ray plates were made by Dr. Bassler himself. We will continue to recommend the book and refer to it in personal work.

T. G. S.

THE URETHROSCOPE IN THE DIAGNOSIS AND TREATMENT OF URETHRITIS. By N. P. L. LUMB, M.D., Major, R. A. M. C. (T. C.). First edition. Pp. 51; 42 illustrations, 39 in color. New York: William Wood & Co.

THE real value of this little treatise, and one in which it is not only unique but a decidedly welcome contribution to our knowledge, lies in the fact that its author has appreciated that you cannot teach the subject by didactic lectures nor by verbal descriptions, and while actual clinical experience is the best of all teachers in the subject, the next thing to such practical instruction is a presentation of the subject by copious illustrations, and in this feature Dr. Lumb's book, with its thirty-nine urethroscopic pictures in color, will ever be a valuable guide to the beginner, the teacher and the specialist.

He unfortunately describes in his brief test (in reality only thirty-eight printed pages) an instrument little known in America, the Wyndham-Powell air-dilating urethroscope, though the conditions he so ably illustrates are true to those seen through any of the instruments in daily use in this country. A. R.

A HAND-BOOK OF GYNECOLOGY. FOR STUDENT AND GENERAL PRACTITIONERS. By BETHEL SOLOMONS, B.A., M.D., F.R.C.P.I.; Gynecologist to Mercer's Hospital, Dublin. Pp. 236; 196 illustrations. New York: William Wood & Co.

THIS book represents a collection of the author's lecture notes which he has endeavored to place before the profession in tangible form. Of course, in a small volume it is manifestly impossible to deal extensively with the various subjects considered, but the author appears to have devoted too much space to academic and unessential classifications at the expense of diagnosis and treatment. The views expressed are in many instances too ancient to allow the book to be considered abreast of the times. Perhaps it is conservatism on the author's part in almost ignoring the value of radium in the treatment of gynecological diseases and in preferring to look askance upon Hirschmann and Adler's monumental work on the endometrium; but when he recommends curettage promiscuously and dilatation of the uterus by laminaria tents we must take exception to such teaching. The illustrations are simple line drawings, but fulfill their purpose. This book may be of great value to the author's own students when supplemented by considerable collateral reading and didactic teaching, but it can hardly be conceived that it would ever appeal to the American student who has been brought up to expect the best in medical books. F. B. B.

PSYCHIATRIC NEUROLOGICAL EXAMINATION METHODS. By DR. AUGUST WIMMER, Director St. Hans Hospital, Roskilde, Denmark. Authorized translation by DR. ANDREW W. HOISHOLT, Medical Superintendent, Napa State Hospital; Professor of Psychiatry, Medical Department, Leland Stanford Junior University, San Francisco, California. First edition. Pp. 172. St. Louis: C. V. Mosby Company.

THIS small book gives an excellent outline of neuropsychiatric examination. For example, when discussing ophthalmoscopic examinations it tells what examination should be made and gives a short explanation in what conditions choked disk, optic atrophy, etc., are found. It does not by any means essay to be a diagnosis.

The book has been well translated and the work is well done, but the reviewer questions whether such a book is of value. The general practitioner will not find it sufficiently explanatory. It cannot, of course, be intended for the neurologist, and the average student will have none of it.

T. H. W.

PRINCIPLES OF HYGIENE, WITH REGARD TO THE GERMAN EMPIRE AND AUSTRIA. By DR. W. PRAUSNITZ, Eleventh, improved and enlarged edition, with 284 illustrations. Munich: J. F. Lehmann. 1920.

THIS is the eleventh edition of this book, containing 671 pages. It is printed on rather soft paper. The text is clear but the illustrations are not as distinct as could be desired, because of the cheap quality of paper used.

Following a brief introduction to hygiene, there is a chapter on the microorganisms. Then the following subjects are taken up in sequence: Air, weather and climate, clothing, baths, soil, water, housing, heating, ventilation, lighting, refuse matter, care of the dead, hospitals, child hygiene, school hygiene, nutrition, infectious diseases, industrial hygiene, race hygiene and social activity of the physician.

In general the book has undergone but slight revision from earlier editions, as indicated by the sub-title and the almost complete absence of advances in so many lines of the practical application of newer discoveries during and since the war. Although the fundamental principles presented in the book are sound, it is a source of regret that the enormous strides in our knowledge during the past five years remain unnoted, except in several minor particulars.

Since all the books by American authors dealing with the subject of hygiene have been kept up to date, and present, in more or less detail, the valuable experiences during the war, Prausnitz's book can have no interest for our readers because the contents of the book are largely out of date.

D. B. H.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Typhoid Fever in the American Army in the Great War.—RUSSELL (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1863) has presented some very interesting statistics concerning typhoid fever. The most instructive of these is a comparison of the actual deaths due to typhoid fever, malaria and dysentery in the Great War with the mortality which would have accrued had the death-rate been the same as in the Spanish-American and the Civil Wars. There were actually 213 deaths from typhoid fever in the American Army between September 1, 1917, and May 2, 1919. Had the Civil War typhoid death-rate obtained there would have been 51,133 and had the Spanish-American War typhoid death-rate obtained there would have been 68,164 deaths. He concludes: "It is evident from these tables, therefore, that antityphoid vaccination, carried out as it was . . . gave a high degree of protection to our forces . . . and reduced the (death) rate not only below the rate for previous wars but also below the rate found in civil life in some of the older States where the entire population is protected by all the sanitary measures of modern life."

Use of Air in Roentgenography.—RAUTENBERG (*Deutsch. Arch. f. klin. Med.*, 1919, cxxix, 296) describes the practical value of introducing air into the peritoneal cavity and then making roentgenograms. The procedure is simple and harmless and, in the four cases of liver disease reported, gave very valuable information. The size and shape, and in general, the consistency of the liver may readily be determined and con-

sequently, in some instances, a doubtful diagnosis may be confirmed. The method was first described by RAUTENBERG (*Deutsch. med. Wchnschr.*, 1914, xl, 1205), but remained unnoticed until 1918, when GOETZE (*München. med. Wchnschr.*, 1918, No. 35, quoted from S. and G.) described it as a new method of diagnosis. SCHMIDT and GOETZE (*Deutsch. med. Wchnschr.*, 1919, xlv, 201) have amplified the method and have carefully described the technic. DANDY (*Ann. Surg.*, 1918, lxxviii, 5, and *Johns Hopkins Hosp. Bull.*, 1919, xxx, 29) describes a new method of unusual value in the study of brain tumors, etc. It consists of the introduction of air into the cerebral ventricles followed by roentgenography of the cranium. The procedure is called ventriculography. PFAHLER (*Am. Jour. Roentgenol.*, 1919, vi, N. S., 371) has shown that air may be used as a means of diagnosing certain bladder conditions. The technical details and many photographs will be found in the articles. The use of air as a partially opaque medium to roentgen rays while yet in the experimental stage has proved of considerable clinical value in the study of certain abdominal conditions, but perhaps of more value in the localization of brain tumors.

Cardinal Principles of Cardiological Practice.—LEWIS (*British Med. Jour.*, 1919, ii, 621) gives a brief statement of the chief diagnostic signs in cardiac diseases essentially chronic. Some of his statements are of interest and importance: (a) "Where there is definite enlargement (of the heart) or aortic disease or mitral stenosis or fibrillation of the auricles, then the safe course for doctor and patient is to attribute any undue distress on exercise to a cardiac lesion." (b) "In young subjects, if there is no such immediate evidence of heart disease as I have named in last paragraph, then a deficient exercise tolerance should rarely, if ever, be ascribed primarily to the heart. To this class belong almost all patients who are supposed to be suffering from 'heart strain' and a large number of patients incipiently infected with tuberculosis or chronically infected by pyogenic organisms." (c) "In elderly subjects, if there is no sign of structural disease but a poor tolerance of exercise, the heart cannot be declared free of disease; on the contrary, the heart should be regarded as the probable seat of mischief. It is, of course to this class that many cases of grave angina pectoris belong; but it also comprises many myocardial cases, in which the chief symptom is not pain but breathlessness or undue fatigue." The indications for bed treatment of cardiac cases are (1) distress when walking leisurely, (2) when active infection is known to be present, (3) when drastic treatment with a digitalis body is required.

Lethargic Encephalitis.—L'HERMITTE (*Ann. de méd.*, 1919, vi, 506), in an article entitled "L'Encéphalite Léthargique," has carefully reviewed the whole subject under the name ophthalmoplegic encephalitis with narcolepsy. The present epidemic seems to have started in Austria in the winter of 1916-17, where the first cases were reported by von Economo. About the end of January, 1918, cases were reported by French and English journals. The reports multiplied rapidly. The cardinal symptoms are ocular paralyses, somnolence and fever. The ocular palsies are often the first symptoms; the III pair is often unaffected, but if affected never totally. The paralysis may migrate from

one eye-muscle territory to another. Somnolence may precede or follow the ophthalmoparesis; it is seldom as deep as coma. It is pathological in that the patients attempt to resist it. Delirium may be present. At times other pairs of cranial nerves are affected, especially the VII and occasionally a transient hemiplegia may occur. Certain motor difficulties as hypertonia, incoördination, asynergia, and tremor may occur. The tendon reflexes depend largely on the area occupied by the nervous tissue changes. Signs of meningeal irritation only occur early in the disease. The cerebrospinal fluid is usually normal. Fever is very variable. Pathologically the changes are most marked in the mesencephalon and especially in the locus niger. The cells of the corpus striatum, optic thalamus and the nuclei of the III, IV, V, VI and VII nerves show slight but definite changes as a rule. The white matter shows no change. There may be widespread dilatation of small blood-vessels with hemorrhagic areas and perivascular infiltrations by cells of various types. The remainder of the article considers the relation between the disease "nona" and lethargic encephalitis and other known forms of encephalitis. The article is a complete *resumé* of the subject to date and is well worth the attention of those interested in the present epidemic.

Specific Aortitis, Prognosis of.—REID (*Jour. Am. Med. Assn.*, lxxiii, 1832) states that the disease is present in 5.5 per cent. of 1919, autopsied cases at the Massachusetts General Hospital. In the 61 instances studied, the Wassermann reaction was positive or suspicious in 45 cases. Shortness of breath and chest pain were present in all of the cases, and on the average symptoms had been present about a year and a quarter before reporting to hospital. Adequate treatment was carried out in very few cases. Iodides and mercury alone did not seem to arrest the process, but more intensive antiluetic therapy seems to produce promising results.

Blood-pressure, Arteriosclerosis and Contracted Kidney.—HARPUDER (*Deutsch. Arch. f. klin. Med.*, 1919, cxxix, 74) has carefully studied the relation of blood-pressure, arteriosclerosis and contracted kidney in 1165 cases. Of these cases all but 17 were past forty years old. He concludes from the study of clinical and pathological material that arteriosclerosis alone does not cause hypertension even if the smaller renal and cardiac vessels are involved. But that renal changes produced by the sclerosis of the smaller vessels lead to arterial hypertension. The appearance of hypertension is independent of the severity and extent of the anatomical lesion. Every patient with persistent hypertension has already a renal injury.

Progressive Hypertrophic Neuritis of the Adult (Non-familial).—ROUSSY and CORNIL (*Ann. de méd.*, 1919, vi, 296) report a case, aged forty-four years, negative personal and family history. Began at forty. Marked atrophy of muscles of arms, with Aran-Duchenne hand and fibrillary twitchings. R. D. in nerves attacked. Ataxia, especially on left; more marked in arms. Romberg +. Intention tremor of arms. Sensibility slightly affected in left hand. Achilles and left patellar jerks absent. Periosteoradial reflexes absent. Pupils normal. Many

peripheral nerves greatly thickened. Section of nerve showed: (1) degeneration of myelin sheaths; (2) proliferation of cells of sheath of Schwann; (3) alteration of axis cylinders; (4) numerous small regenerating axis-cylinders; (5) hyperplasia of connective tissue. Wassermann reaction in C. S. F.+. The case differs from the Marie or the Déjerine type.

The Tarisch-Herxheimer Reaction.—HESSE (*Wien. klin. Wchenschr.*, 1919, xxxii, 439). The Herxheimer reaction is not characteristic in the sense that it is specific either for lues or for a certain drug, because it may occur during the treatment of non-specific dermatoses by mercury. This is proof that the reaction is not due to the flooding of the blood by endotoxins produced by the sudden death of large numbers of spirochetes. The reaction may be due to the injury of endothelial cells by the drug used.

Cerebral Disturbances Following Wounds of the Carotids.—ROHARDT (*Deutsche Ztschr. f. Neuroh.*, 1919, lxiv, 39) says that the fatality in carotid wounds usually results from hemorrhage or from anemia, and one seldom sees the cerebral complications. The mortality is about 50 per cent., but sinks to 10 per cent. under favorable conditions, that is, when early ligation can be done without infection. Death is due to anemia of one hemisphere. In many instances, after an interval, sometimes of several weeks, symptoms of a cerebral lesion appear. In general about two days elapse. The area of softening depends upon the adequacy of the collateral circulation. If the carotid is only partly occluded, the early functional disturbances may recede. Two of the cases reported had neck wounds and cerebral disturbances without obvious carotid wounds. In one of these there developed a carotid aneurysm, in the other a partial thrombosis. In both instances the cerebral symptoms were due to emboli. In the other two cases the carotid was ligated. In one there developed a left VII paresis, paresis and tactile agnosia of the left arm, apraxia of the left hand and a pseudobulbar speech defect. In the other case a period of six weeks elapsed before the appearance of a right optic atrophy and Horner complex.

The Pathology of Commotio Spinalis.—JAKOB (*Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1919, li, 247) states that the *commotio spinalis* and *contusio spinalis* merge one into the other. A soldier had a through-and-through abdominal wound at the level of the XII dorsal vertebra, with sensory and motor paralysis below L. seg. III. There were lesions of more than one spinal segment, *i. e.*, the sensory and motor disturbances were different at different levels. Sudden death from rupture of traumatic abdominal aortic aneurysm. Autopsy, a slight comminution of the XII dorsal lateral process. The cord showed diffuse nerve fiber degeneration in the white matter of the sacral and lower lumbar region; marked swelling of the tissue; many necrotic patches in the gray matter; ganglion cell changes and glia proliferation. A few small hemorrhages. The entrance zones of posterior roots showed changes. The author thinks this instance supports his and others experimental and clinical conclusions that the symptoms in *commotio* are due to actual traumatic lesions of cord rather than to hemorrhage.

SURGERY

UNDER THE CHARGE OF

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The Good Surgeon.—CRILE (*Ann. Surg.*, 1919, lxx, 385) says that the surgeons and pathologists who for years have intensively studied war wounds have formulated many theories of treatment—many apparently contradictory theories. He thinks that out of the present wide divergence of opinions the same fact that emerged from the post-Listerian period is emerging now—that the one agent of successful surgery is the good sound surgeon. Sound surgery means quick, innocuous, timely intervention; it means clearly the tomorrow of the wound; it means no intervention unless there is to be a net gain; it means a sharp knife, a good anesthetist, a painless, innocuous dressing.

Roentgenography of the Brain after the Injection of Air into the Spinal Canal.—DANDY (*Ann. Surg.*, 1919, lxx, 397) has previously shown that the cerebral ventricles can be outlined by a roentgenogram if injected with air. When doing this he noted that in many cases air could be seen in filaments on the surface of the brain. This must have followed the normal pathway by which the cerebrospinal fluid circulates. These observations gave promise of new possibilities in intracranial diagnostic study, because many lesions of the brain affect part of the subarachnoid space directly or indirectly. By substituting air for cerebrospinal fluid through a lumbar puncture all parts of the subarachnoid space can be clearly seen in a roentgenogram. Not infrequently an air shadow will completely surround the cerebellum, showing clearly its shape and size. The spinal cord can also be surrounded by a column of air. If the subarachnoid space is intact the air will always fill the cerebral sulci if given by an intraspinal injection. Frequently the exact position of the obstruction in the cisternæ can be seen in the radiogram. By its use one can detect whether or not a case of hydrocephalus is of the communicating type or not. This procedure is not devoid of danger if the amount of air is in excess of the fluid withdrawn, and this is especially true of intraspinal injections. The position is especially important, the head being at least 20 degrees higher than the needle.

Fracture of the Skull, with Special Reference to its Neurologic Manifestations.—WILENSKY (*Ann. Surg.*, 1919, lxx, 430) reports 75 cases of fracture of the skull admitted to Mt. Sinai Hospital, New York, where neurological cases, including skull fractures, have been segregated into a separate service. The great majority occurred in the first decade of life, and there were three times as many in the male as in

the female sex. The actual mechanism has almost always been a direct blow. The extent of the fracture varied greatly. Many were bursting fractures, probably, from direct impact through the lower jaw. Of the locations determined through the roentgen ray the most frequent sites were the parietal, frontal, frontoparietal and parieto-occipital regions. Most were simple fractures, but they frequently involved more than one of the bones. The fissures were usually vertical or oblique behind the coronal suture, those in front of the coronal suture running downward and forward toward the anterior cranial fossa. In one of the cases the edges were separated so far as to allow the dura to project between them. Comminution with depression was present in 8 cases. In the cases coming to operation the subjacent brain was often found to be injured with or without laceration of the overlying dura. The brain damage often exceeded that of the skull. One case demonstrated the contre-coup mechanism. Roentgenographic studies were made of all cases, except those admitted in a moribund condition. The symptoms of brain irritation were not always present. The variation of symptoms was wide, vomiting and headache being the most frequent. In all cases except those with scalp wounds which disclosed fractures only by the roentgen ray, there was a transient or persistent loss of consciousness. This depended upon the degree of concussion or compression. A number of cases developed fever without any apparent source of infection, the highest temperature being 109° F. This was probably due to brain trauma. The general neurological symptoms were varied. Twelve patients died of concussion within a few hours of the accident. Compression phenomena were common and usually appeared quickly. In judging the severity of the increase in intracranial pressure, the greatest reliance was always placed on the condition of the circulation, and a marked increase of pressure was the most imperative indication for operation. Generalized convulsions were present in only 1 case. The reflexes were frequently altered, but often had no bearing on the total clinical picture. Thirteen cases showed abnormalities of the external or internal ocular apparatus. Three cases had unilateral exophthalmos. Eleven had abnormalities of the fundi. The cranial nerves were involved in 7 cases, the orbital in 2 and the facial in 5 cases. Focal symptoms of the extremities were present in 4 cases. The longitudinal sinus syndrome, a spastic paraplegia, was present in 6 cases. In all these cases the injury was near the vertex. Various complications, such as intracranial hemorrhage, leakage of cerebrospinal fluid and meningitis were met. It was not considered imperative to operate on all compound fractures, except to debride the wounds. According to the symptoms exhibited, unilateral or bilateral exploratory craniotomy or a craniotomy plus a contralateral subtemporal decompression was performed. Lumbar puncture was not done routinely, as it did not seem to give any added information. Of the 72 cases, 22 died (31 per cent.). Eighteen were operated on, with a mortality of 48 per cent. Of those treated conservatively the mortality was 27 per cent. Wilensky does not think that operation, skilfully done, adds anything to the risk. Conservative and expectant treatment, whenever they can be safely employed, yield the best results. Operation is imperative in every case showing signs of increasing intracranial pressure, as irritative or paralytic focal symptoms.

Treatment of Chronic Empyema.—WATTENBERG (*Ann. Surg.*, 1919, lxx, 552) reports the results of treatment in 121 cases of chronic empyema at General Hospital No. 26, Fort Des Moines, Iowa. Practically all the cases in this series had had an operation, most commonly rib resection, before admission. The following factors were of vital importance: Adequate drainage was accomplished in some cases by dilation of an already existing sinus by the introduction each day or two of a slightly larger drainage tube than that previously in place. This dilation was continued until the tract was of sufficient size to admit six to eight Dakin's tubes and at least one overflow drainage tube one-quarter inch in diameter. In cases in which the density of the scar tissue above the sinus or the reformation of the resected rib had closed the opening to such an extent that an ample opening could not be obtained, an operation was performed. An incision was made along the course of the rib above the sinus and the rib was resected for a distance of two to two and one-half inches. Any bone interfering with drainage was removed. The pleura was found to be thickened by a tough, fibrous exudate. It must be excised to obtain competent drainage. Simple incision through a thickened pleura is followed by too rapid healing to ensure a good result. In certain cases this organized exudate practically filled the cavity. It was dissected out with the fingers and removed. Dakin's tubes and overflow tubes were then inserted and held in place by gauze tightly packed into the external orifice of the wound. The next factor after drainage was the careful sterilization of the cavity by the installation of Dakin's fluid. The whole cavity was flushed out once a day by the chlorin preparation. The cavity was filled to overflowing with this solution every hour by day and second hour by night. The patient was instructed to shift his position freely during each instillation. The skin was carefully protected against burning by the solution. The sterilization of the cavity was determined by bacterial controls taken twice a week. When a cavity was found to be sterile on seven successive days, the tubes were removed, gauze tightly packed into the external orifice and the cavity permitted to close. The streptococcus hemolyticus was found in 100 per cent. of cases. The cavities never closed spontaneously while this organism was present, but often did so (62 cases) after this organism had disappeared, though other bacteria were still present. Wattenburg thinks that a bronchial fistula is no contra-indication to the use of Dakin's solution. By careful handling the fistulae healed under this treatment. The third essential factor in the treatment of chronic empyema is high caloric feeding. Blowing exercises with Wolfe's bottle and graduated calisthenics aided in the expansion of the chest on the affected side. In all 201 cases were treated. All but 27 healed under the treatment outlined. Three of these closed permanently two months after the tubes were withdrawn. Two were definitely tuberculous and three are still under treatment without drainage. Seven are receiving further Dakin treatment. Three died. Twelve were transferred to other hospitals before this treatment was completed.

Infections of the Knee-joint.—ORR (*Surg., Gynec. and Obst.*, 1919, xxix, 492) found that knee conditions in France presented themselves in two principal forms: (1) The so-called internal derangements, and

(2) the acute infections. He deals with the second group, which he divides into four varieties: (1) Acute infections of the joint, with the formation of pus but no opening into the joint; (2) compound injuries to the joint but no damage to the bone; (3) compound fracture of the femur or tibia involving the joint; (4) cases included in 2 or 3, with general sepsis supervening. In cases of the first variety, active and passive motion to an extent not causing pain, can be used after adequate drainage has been instituted. In only a few cases of the second variety and in no cases of the third and fourth varieties should an attempt be made to secure a movable knee-joint. Ankylosis is the end to be sought, with the knee at an angle of from 10 to 20 degrees. Attempts to secure motion except by late arthroplasty should be discouraged, except in group one.

THERAPEUTICS

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Local Serotherapy of Gonococcus Rheumatism.—DEHRÉ and PARAF (*Bull. de la Soc. méd. des. Hôp.*, 1919, xliii, 908) describe in detail 15 cases of acute gonococcus arthritis treated by injections of antigonococcus serum into the affected joints. In 6 cases the cure was complete in less than eight days; in 8 others before the fifteenth day. The joint function returned to normal in a rapid and apparently complete manner. This treatment is limited to the larger joints because of the difficulty of injecting the serum into a small joint. They puncture the joint and inject the serum in place of the effusion. This was repeated every day or every second or third day. In the case of multiple joint affections they were all treated at the same time in the same way.

Harmful Effects of Shallow Breathing, With Special Reference to Pneumonia.—From observations on a number of cases of pneumonia, MEAKINS (*Arch. Int. Med.*, 1920, xxv, 1) concludes that the anoxemia occurring in acute lobar pneumonia is the result of the rapid and shallow breathing typical of this condition. It is well known that the severity of the symptoms in pneumonia is not necessarily dependent on the degree of pulmonary involvement. A much more valuable indication as to prognosis is the respiratory-rate. It has been observed that as the respiratory-rate increases the patient's condition becomes more grave. As a rule, in adults when the respiratory-rate persists above 50 per minute, cyanosis begins to develop. This is a definite sign of pronounced anoxemia. The harmful effect of persistent anoxemia on

the cardiovascular system is well recognized. There is no particular proof that the cyanosis in pneumonia is due to cardiovascular failure, and careful observation leads the author to believe that the cardiovascular collapse is a sequel to the anoxemia. In spite of the gradual increase in the total volume of expired air per minute there is a very conspicuous diminution in the ratio between the respiratory volume and the theoretical dead space until a point may be reached where the alveolar air, expired or inspired, amounts to comparatively few cubic centimeters, being undoubtedly insufficient to carry on any adequate pulmonary ventilation, so that eventually cyanosis develops. The respiratory quotient becomes progressively higher, but when the crisis occurs there is a rapid return to normal not only in regard to the respiratory quotient but also in the respiratory-rate and volume and the total ventilation per minute. Another aspect of the question is the part played by the pulmonary circulation. While it must be assumed that a certain volume of blood passes through the damaged lung area without proper ventilation, we are not justified in supposing that this non-ventilated blood is sufficient in amount to reduce appreciably the oxygen content of the mixed blood entering the left side of the heart. Therefore the author concludes that the anoxemia occurring in pneumonia is the result of the rapid and shallow breathing.

Acute Methyl Alcohol Poisoning Associated with Acidosis.—HARROP and BENEDICT (*Jour. Am. Med. Assn.*, 1920, lxxiv, 26) report a case of severe acute poisoning with methyl alcohol associated with a marked grade of acidosis, in which recovery followed the use of alkali therapy. The acidosis was associated with an increase in the amount of titrable organic acids in the urine and specifically with a marked increase in the excretion of lactic and of formic acids. The authors cite an observation of Bongers, who gave methyl alcohol to dogs by mouth and was able to recover about three times as much methyl alcohol in the combined washings of the second and third days as he was able to obtain in those of the first. This work would appear to clearly indicate the importance of thorough and repeated lavage.

The Basal Metabolism in Exophthalmic Goitre.—This paper by MEANS and AUB (*Arch. Int. Med.*, 1919, xxiv, 645) is based on 345 metabolism observations on 130 patients. These observations bear out the conclusions drawn in their first paper on the subject. In addition, using the basal metabolism as an index of toxicity, they find that: (1) In the majority of cases the results after two or three years are equally good with roentgen-ray treatment as with surgery. (2) After surgery the metabolism shows a rapid preliminary fall, a secondary rise followed by a final fall; with roentgen-ray treatment there is a gradual progressive fall. (3) In securing the same end-result with surgery or with the roentgen ray, a lesser rest factor is necessary with the latter. With the roentgen ray there is practically no mortality; with surgery there is a definite one. (4) Patients treated surgically do better and the risk of operation is less, if they have previously had their thyroid and thymus glands irradiated. (5) The risk of operation

is greater and the need for preoperative roentgen-ray treatment is greater in cases with a very high metabolism and moderate tachycardia than in those with an extreme tachycardia and moderate metabolism elevation. (6) The safest program for the treatment of exophthalmic goitre, as a whole, is the routine irradiation of thyroid and thymus glands, in all cases, with surgery held in reserve for patients who do not then do well. (7) Surgery is contra-indicated with patients whose metabolism is rising in spite of complete rest in bed, and also with patients of the type with moderate tachycardia and great metabolism increase, except when they have previously had thyroid and thymus glands treated by the roentgen ray. (8) Finally, they believe that in the management of exophthalmic goitre, periodic determination of the basal metabolism should be quite as much a routine as is the examination of the urine for sugar in diabetes mellitus. Further, in border-line cases they believe the basal metabolism furnishes very valuable aid in differential diagnosis.

PEDIATRICS

UNDER THE CHARGE OF

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Thymus Study.—PARKE and McCLURE (*Am. Jour. Dis. Children*, November, 1919) have made an exhaustive review of the literature on the thymus gland and also publish the results of their own experiments, comparing the work of their predecessors with their own. Their work was undertaken in the belief that it was possible to produce in animals a rickets almost, if not quite, identical with human rickets by means of the removal of the thymus gland. As regards the former literature it is doubtful whether an unprejudiced person who read for the first time the articles on extirpation of the thymus, could obtain from it any clear conception as to what the effects of removal of the thymus actually are. He would probably be at a loss to know whether to regard the thymus as essential to life or as an organ devoid of function, or at least of function demonstrable by extirpation. Unfortunately the more recent experimental work on thymus function has not brought the problem any nearer solution. Indeed it has been productive of more widely divergent results than the earlier work. Some of the causes of the confused state of our knowledge concerning the effects of the removal of the thymus may be laid to the fact that a large amount of the experimental work connected with extirpation of the thymus has been inadequate. The experiments of the earlier and more recent investigators who have depended for the removal of the thymus on the method originally employed by Friedleben, cannot be accepted as valid for the determination of the function of the thymus, for if extirpation performed by that method is even approximately complete, it cannot possibly be so with any regularity. The experiments of others who employed better operative methods are of little value or actually worthless because of

the careless manner in which they were conducted, the use of unsuitable experimental subjects, the lack of sufficient control animals. It is also apparent that a number of investigators have drawn conclusions in regard to the effects of removal of the thymus from experimental data which are wholly inadequate, and have not only increased the number of erroneous conceptions, but have planted them firmly in literature. Soli, for example, inferring that the thymus exerts a regulating influence over the growth of bone in very young but not in older animals, as the result of one experiment on a rabbit two months old, or Seimhuber stating that the thymus is non-essential to life from experiments on two dogs, neither of which appeared to have been necropsied in order to make certain that the extirpation had been complete, are only two of a number of possible illustrations. Experiments so limited that chance variation of dietetics or environmental influences cannot be excluded as the controlling factors do not prevent of any induction concerning thymus gland function. Few seem to have hesitated to draw hard and fast conclusions of inadequate facts. It is also manifest that a number of investigators have placed overvaluation on positive experimental results at the expense of negative experimental results. Those who have done this seem to have started out with the assumption that the thymus possessed a function susceptible of demonstration by means of extirpation, and that negative results are, from the very nature of things, meaningless. Accordingly in forming conclusions they have considered only positive results. It must be clear to everyone that in this particular field of investigation the positive experimental results which have been obtained do not have more significance than the negative results, inasmuch as they have not consisted in the development of changes in thymectomized animals which are not specific but may be brought about in other ways than by the removal of the thymus gland, or may develop spontaneously. In this way it has come to pass that a discrepancy has arisen between the actual results of the experiments themselves and the conclusions drawn from them, which appears not on the surface but becomes apparent after study of the experimental literature. If only conclusions which investigators have drawn from their experiments are considered, as is the case in almost all discussions or presentations of the thymus problem in the literature, a false impression as to the actual experimental results is obtained. The causes reviewed above in explanation of the confusion of ideas which exists concerning the effects of thymus extirpation cannot be regarded as having been more than contributing factors. Undoubtedly the fundamental cause lies in the difficulties inherent in the problem itself. The diverse character of the results from the same procedure is sufficient proof that either the elicitation of evidence of thymus function is exceedingly difficult, or else that the thymus is possessed of no function or of no function that is demonstrable by extirpation. The only certain knowledge in regards to the removal of the thymus up to the present time afforded is surprisingly small and may be stated as follows: The thymus is not essential to life in the frog and its complete removal from that animal causes no alteration in bodily growth or development; similarly the function of the thymus gland is not necessary to life in the rat and its destruction in that animal produces no demonstrable alteration in growth or development or any changes of a morphological nature

in any of the organs, as judged by the ordinary methods of histologic study. Few of the positive results of thymectomy have actually been proved to be false. It is certain only that the remarkable train of symptoms ending in death which Abelous and Billiard, and later Camia, announced they obtained in the frog, and those of Magini, Klose, Fleisch in the rat, must have been due to other causes than deprivation of thymus function. The reported results of thymectomy fall roughly into three groups: In one, removal of the thymus has been found to be without effect; in another removal has been followed by transitory disturbances in health and development; in the third removal has brought about death with or without changes in growth and nutrition, and alterations in the skeleton, and in certain of the organs, particularly those of internal secretion. A considerable number of observers have been unable to detect any change, or at least, any change of significance following thymectomy. Comparatively few have discovered that removal of the thymus produced death, and not a single one has found that thymectomy caused death invariably, or even in the majority of cases. Almost all of those who have reported positive results following extirpation of the thymus, have obtained negative results as well, the two kinds being intermingled in varying proportions. Though the changes reported by some have been limited to single pathological manifestations or to alterations in a single organ and have seemed to indicate that thymus activity was distinctly circumscribed, the changes reported by other investigators, particularly some of the more recent, have been in the nature of complex diseased states in which the whole animal was affected, and have seemed to imply that the function of the thymus was intimately concerned with the most fundamental of the bodily functions. The positive results obtained by some investigators seem to have little connection with the positive results obtained by the others, and in a few instances have been contradictory. Those obtained by some have a certain amount of similarity in that they center about changes in the growth and development of the skeleton such as overgrowth of the animal as a whole an increased growth of the skeleton; retardation in growth of the skeleton; retardation in growth with thickening of the bones of the skeleton; thickening of the bones with bowing; spontaneous fracture; reduced calcium content of the bones; pseudo-rachitic deformities; osteoporosis; osteomalacia; rickets. At least nine investigators have described in one or more thymectomized animals retardation in growth with rachitic-like deformities, especially in the long bones of the legs. Only two of them have given proof that the pathologic condition in the bones of their experimental animals was really rickets. One has shown on fairly good evidence that both the thymectomized and control animals of his experiments were affected alike with rickets. Several observers have reported alterations in the hair of their thymectomized animals, and several have described a voracity of appetite exhibited by the thymectomized animals in contrast to their control mates. A very few investigators have examined their material for alterations in the endocrine glands. Five have reported changes in the nature of hyperplasia in the thyroid and two have reported hypertrophy of the medulla of the suprarenal, but no one has reported pathologic developments which are of a convincing character in any of the other organs of internal secretion. Few seem to have studied the organs

of internal secretion with any care and no one has applied to the study some of the more recently developed histologic methods or made examinations in the period which immediately followed thymectomy. As a result of their own studies the authors show that the thymus gland is not essential to life in the dog. Extirpation of the thymus produces no detectable alteration in the hair, teeth, contour of the body, muscular development, strength, activity or intelligence of the experimental animals. Extirpation of the thymus probably does not influence growth or development. The possibility that it may cause retardation in development and delayed closure of the epiphysis cannot be excluded absolutely. Removal of thymus probably produces no alteration in the organs of internal secretion. It is possible that it produces well marked changes in the organs of internal secretion in the period immediately following thymectomy, an observation that was not covered by these investigators in their series of experiments.

Human Rabies.—REGAN and SILKINAN (*Arch. Diag.*, April, 1919) discuss this important topic from the standpoint of their recent experience. They found that the best method of treating the bites of suspected rabid animals is by cauterization. Many writers advocate the various caustics indiscriminately considering all of equal value. This is important as many of the more commonly used methods, such as cauterization with carbolic acid, silver nitrate and the thermocautery are objectionable in that they seal up the virus by coagulating the albumin of the tissue cells. Nitric acid does not possess this very serious disadvantage for by virtue of its power of diffusibility and penetration, it may destroy the virus in cases in which the other methods would have no results. It is especially valuable in the cauterization of bites treated late. It produces little scarring and the resultant wound heals well. It is the caustic that should always be employed. To get the utmost effects the nitric acid must be fuming. The wound should be cauterized as soon after the bite as possible. While many writers claim that to be effective cauterization must be employed within the first few hours after the bite, there is no experimental proof to show that certain caustics, notably nitric acid are effective at a much later period. Hence in cases in which the bite is seen late, nitric acid should be applied even up to the seventy-second hour after the accident. This is logical because it is well recognized that the virus progresses very slowly from the original atrium of infection. If only part of the effective material introduced is destroyed, the amount may be sufficient to allow the body to overcome the small portion of the virus unaffected by the cauterization. Prior to cauterization the wound should be squeezed to encourage bleeding and should be thoroughly washed with mercuric chloride solution 1 to 1000. A wet dressing of the same should be applied after the caustic has been used. If the wound is a punctured one and cannot be properly cauterized, it should be laid open with a scalpel to allow treatment. A bite should not be sewed up. If sutures have been introduced before the patient appears for treatment, they should be removed and cauterization performed. For ordinary bites nothing stronger than a three-day cord should be used. For face bites and extensively deep wounds a two-day cord should be employed. If the patient has been bitten by a positively rabid animal it is a practice to

advise a return for a second series of injections after six months. This will prevent those rare instances of death when the particular virus concerned has a long incubation period. In the case of face bites or very extensive wounds one of the writers of this paper has recently recommended that the entire course of treatment be repeated two weeks after the completion of the first.

GYNECOLOGY

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Trigonitis in the Female.—There is a large and common group of cases, in which the symptoms are chiefly those of bladder irritability with a clear urine and no gross intrinsic or extrinsic pathology to explain them. In these cases careful examination with the cystoscope will reveal definite changes in the trigone as the chief pathological feature and to this group of cases we apply the term cystitis colli or trigonitis. The onset is generally insidious with gradually increasing frequency of urination, especially by day, but somewhat also at night. With this there is usually no pain, but at the end of the act of urination there is generally a sensation of incompleteness and a desire to pass more. The patient will empty her bladder and within two or three minutes have an uncontrollable desire to urinate again which usually, if yielded to, accomplishes nothing or at most only a few drops are expelled. There is an almost constant desire to urinate and many patients complain that by day they are obliged to relieve themselves as often as every five minutes, voiding only a few drops each time. In the later stages there may be some pain but it is rarely very severe, and occasionally there may be a slight terminal hematuria. The treatment of these cases has always been more or less unsatisfactory, although many varieties of treatment have been advocated. The latest treatment of this condition, as described by LINDEMAN (*Surg., Gyn., and Obst.*, 1920, xxx, 64), consists of the injection of quinin and urea hydrochloride into the bladder mucosa. This treatment is based on the well known fact that this drug, when injected into the tissues, especially in a strength of over 1 per cent., causes a deposit of fibrin and a considerable induration at the point of injection which not infrequently remains for months. Furthermore the outstanding feature of the cystoscopic picture of this disease is intense congestion, hypertrophy and hyperplasia of the subepithelial bloodvessels and the swollen mucosa. Therefore Lindeman deduced that if anything could cause the destruction

or at least constriction or compression and thereby reduction in size and possibly in number of these bloodvessels, the disease would be relieved and he felt that the injection of quinin and urea hydrochloride could accomplish these objects. He uses a sterile 2 or 3 per cent. solution of the drug in normal saline solution colored with methylene blue (for technical purposes) and makes the injections by means of a very long flexible needle which is introduced into the bladder through the catheterizing channel of a cystoscope. The needle is inserted into the mucosa of the trigone, preferably near one of the ureters, and a few drops of the solution are injected, producing a small blue wheal. The needle is then inserted into other areas of the trigone and the process repeated until as much of the trigone as possible has been injected. He states that practically all of the patients that have had this treatment have been greatly relieved and many of them required no further treatment. There is one possible danger of this treatment and that is the tendency of this drug to cause necrosis of the tissues when injected under pressure, but thus far Lindeman has had no such untoward result although he realizes the possibility of this outcome.

Ruptured Ovarian Cyst Without Symptoms.—Rupture of ovarian cysts is not, of course, extremely rare but from the clinical standpoint the case reported by BEVAN (*Surg. Clinics of Chicago*, October, 1919, p. 1083) is of interest because there was a complete disappearance of a very large tumor without any symptoms. The patient was a woman, aged thirty-five years, who had been married a number of years but had never had any children. On examination she presented a large cystic tumor of the abdomen which was diagnosed as an ovarian cyst and operation was strongly urged. About two weeks later she returned and stated that the tumor had disappeared, that her clothes were four inches larger than they were before and that she had lost eight or ten pounds in weight. Examination at this time confirmed her statement as the tumor had completely disappeared and there was not even any mass palpable on bimanual examination. Bevan suspected a ruptured cyst and sent her to the hospital for operation and when the abdomen was opened a cyst of the left ovary was found which contained between two and three quarts of yellowish fluid and at one point the cyst wall was very thin and adherent to the cul-de-sac and Bevan believes that it was at this point that the cyst had ruptured. The total absence of symptoms, either at the time of rupture or subsequently makes this case an interesting rarity.

Ovarian Residue in Therapeutics.—For some time GRAVES (*Surg., Gynec., and Obst.*, 1919, xxix, 537) has been advocating the use of ovarian residue in the treatment of those conditions which are usually attributed to deficient ovarian secretion. By the term ovarian residue he refers to that part of the ovary which remains after ablation of the corpus luteum and which has usually been discarded as valueless. The results that he has attained with ovarian residue so closely parallel the effects obtained from whole ovary that it has been impossible to draw any definite conclusions in favor of one or the other preparation. He feels safe in stating, however, that the ovarian secretion is not solely confined to the corpus luteum since the secretion of the atretic follicles

and the corpus luteum is a similar product being manufactured by analogous cells, namely by those proliferated from the internal theca. Ovarian residue preserves its integrity longer than do those ovarian preparations which contain corpus luteum substance so that under present conditions of preparation ovarian residue is in general superior in its clinical results to the commercial articles now on the market. The case reports which are included in his articles are divided into three groups: (1) those exhibiting the symptoms of the artificial or natural menopause; (2) those treated for such menstrual disturbances as amenorrhœa, oligomenorrhœa, delayed menses and clotting; (3) those of essential dysmenorrhœa. The majority of the cases of the first group were treated for postoperative hot flushes. In only a few of the cases were the symptoms severe, and in many they were not a source of complaint, being elicited only after questioning the patient. Ovarian residue was administered therefore, in many instances chiefly for the purpose of testing its effects on these characteristic vasomotor manifestations. For hot flushes, ovarian residue like the other ovarian preparations, acts as a specific palliative rarely failing to give some relief. For those multiple neurosecretory disturbances such as dizziness, sleeplessness, headaches, muscular pains, buzzing in the ears, asthenia, etc., which are so common in the natural, though not in the artificial menopause, ovarian residue is helpful in many cases. In this group there were 41 cases and the treatment exerted a beneficial action in 32 or 78 per cent. In the second group there were failures, especially in the long standing cases of amenorrhœa, although in some instances of delayed menses and clotting the results were rather striking. Even in the amenorrhœa cases in which the menstrual rhythm could not be reëstablished, the patients often mentioned the tonic effect of the treatment. The third group of essential dysmenorrhœa is quite incomplete since he has only recently used the residue in the treatment of this important disorder. Although he is now treating a number of dysmenorrhœa cases of the anteflexion type with the hope of avoiding operative interference, sufficient time has not elapsed to warrant definite conclusions.

Indications for Sterilization.—In considering the question of when sterilization in women is justifiable, PETERSON (*Jour. Mich. State Med. Soc.*, 1919, xviii, 608) calls our attention to the fact that there are two kinds of artificial sterilization of women—primary artificial sterilization and incidental artificial sterilization. In primary artificial sterilization, the end in view is solely to prevent future conception. Incidental artificial sterilization means the sterilization of the woman during the course of another operation in the belief that the patient's life or well-being would be seriously impaired by future pregnancies. Primary artificial sterilization should be comparatively infrequent, since the organic disease which calls for the operation at the same time renders it hazardous and in the uncertainty of the woman with organic disease requiring sterilization, the physician will hesitate to advise this procedure when the uterus can be emptied with less danger in case pregnancy supervenes. In incidental sterilization, the woman can be rendered sterile by a simple additional operative technic the dangers of which are practically *nil*. Peterson believes that all operations devised for temporary artificial sterilization are based upon wrong premises, since

the indications calling for sterilization are bound to grow worse, never better. As a rule a woman should never be sterilized without her consent and that of her husband, and of her family or other physician. Finally, careful study of the history of the patient, especially her puerperal history, her past and present condition, will enable the physician to decide for or against primary and incidental artificial sterilization in pulmonary or other forms of tuberculosis, diseases of the kidneys or heart, mental diseases, pelvic contraction, defects in the reproductive organs due to previous labors or operations, and operations of such nature that subsequent pregnancy and labor are rendered dangerous.

PATHOLOGY AND BACTERIOLOGY

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The Size of the Spleen in Immune Mice.—Although the literature is full of articles upon the part played by the spleen in the growth and development of tumors, it will be found that there is no evidence so far advanced for the significance of the spleen in resistance that cannot be matched with equally good evidence against its participation. WOGLOM (*Jour. Cancer Res.*, 1919, iv, 281) gives a brief review of the chief arguments as a preface to his work on this much debated subject. Underlying all the reports of an hypertrophied spleen in tumor-bearing or immune mice is the tacit assumption that the organ was of normal size before inoculation. However, a careful study of mice and the most common mouse infection (mouse-typhoid) will reveal the fact that very few strains are free from this disease and consequently mice which are generally considered normal have enlarged spleens. The author performed a series of experiments on mice to determine the average weight of a normal spleen. The direct measurements of the organ were made by laparotomy and in order to determine whether or not the spleen enlarged after the operation two sets of animals were autopsied two and seven weeks after the incision and first measurements were made. It was found that of the two-week animals 20 per cent. developed an hypertrophied spleen and of the seven-week 50 per cent. showed a still greater enlargement of this organ. The author makes allowances for both cage infection and infection at operation but is unable to come to any definite conclusions from the data at hand. He thinks it fair to assume that laparotomy does not result in enlargement of the spleen, when done with reasonable cleanliness. After extensive experiments in which mice were inoculated with various immunizing and non-immunizing materials the author is unable to adduce any positive results. The presence or absence of an enlarged spleen in natural, as in acquired immunity, is a matter of pure chance so far as susceptibility or resistance to tumors is concerned. Splenic enlargement therefore is certainly

the effect of extraneous factors and can often be traced to mouse-typhoid. The author is not able to bring forward any argument to refute that of those who believe that the lymphocyte plays an important role in establishing a tumor immunity. He thinks the spleen might be actively engaged and yet not show participation in so far as its size is concerned. All his experiments reveal only the fact that some immune mice have enlarged spleens and some have not; some animals with progressively growing tumors have enlarged spleens and some have not. And the existence of other causes of splenic hypertrophy, such as mouse-typhoid, transfers the burden of proof to those who assert that splenic hypertrophy is referable to immunity.

Dissemination and Destruction of Typhoid Bacilli Injected Intravenously in Normal and Immune Rabbits.—STONE (*Jour. Infect. Dis.*, 1919, xxv, 284) presents the results of investigation of the mechanism of destruction of typhoid bacilli in rabbits. The author reviews the different phases in the development of the knowledge of the typhoid bacillus in its various relations to the animal organism. Rabbits were injected through the ear vein, with measured quantities of living typhoid bacilli. It was found that injection of typhoid bacilli into normal animals was followed in a small percentage of cases by fatality. The typhoid bacilli were demonstrated in all organs within one-half hour, and persisted for about fourteen days, with the exception of the gall-bladder, where they persisted beyond the eighty-sixth day. Immune animals' blood and tissues were found to be sterile within twenty-four hours after a similar injection. Repeating the work of Bull and others, similar paradoxical results were obtained, showing the bactericidal property of normal serum and the lack of same in the serum of immune animals *in vitro*, regardless of the agglutinating titre. Addition of leukocytic suspensions to immune serum *in vitro* in the presence of *B. typhi*, produced no inhibition of bacterial growth. Reactivation of immune serum by the addition of fresh normal serum in the presence of *B. typhi*, showed increased inhibition of growth relative solely to the amount of fresh serum added. Admixture of macerated tissue from immune animals to broth suspensions of typhoid bacilli, produced no inhibition of growth. Details of technic are given.

On the Mechanism of Bacterial Infections, with Special Reference to Gas Gangrene.—BULLOCK and CRAMER (*Report of Imperial Cancer Research*, 1919, vi, 23) have carried out an extensive research for determining the critical factors associated with gas gangrene. Gas gangrene, they state, is a "severe local lesion accompanied by a toxemia and followed frequently by a septicemia." The organisms chiefly responsible are *Bacillus welchii*, *Bacillus edematiens* and *Vibrio septicus*. The experiments which were carried out in mice showed that the mere presence of these organisms in a wound is not sufficient to cause the peculiar tissue reactions. Thus when the *Bacillus welchii* obtained from cultures, is washed free from the medium and by-products and is then injected into animals, no reaction of the nature of gas gangrene is obtained. But when the organisms are inoculated along with the medium in which they have grown, the typical gangrene results. The culture medium contains the toxin which assists invasion. The authors

lay stress upon the "specific" effect of the toxin upon the adrenals, which they believe is most important in relation to the fatal outcome. Various factors (cold, exhaustion, fatigue, hemorrhage and anesthesia) place an extra strain upon the adrenals and may further assist in enhancing the influence of the toxin. The toxin of gas gangrene has two separate functions. At first it acts locally in the manner of an aggresin and enables the bacteria to establish themselves in the body; later it produces a specific toxemia which with other factors contributes to the lethal issue. In the ordinary mode of infection by these organisms toxin is not immediately available to permit invasive localization. Small numbers of these bacteria alone will not cause gas gangrene. The authors have found that the accessory factor in establishing the progressive infection lies in the presence of calcium salts which are so commonly introduced in war wounds with the infection. Other substances were also found to act in a similar but less active manner. Contact between the bacteria and the calcium salt is not essential. Gas gangrene will develop if the bacterial suspension and the calcium salt are injected at different times into the same site or into different sites at the same time or at different times. The calcium salts produce a local change in the tissues disturbing the defensive mechanism against these bacteria. Injury of muscle tissue is not essential for the development of gas gangrene. The authors explain the manner of the action of calcium salts as follows: "One factor which determines the course of an infection is related to the mechanism by which the leukocytes are first guided to the focus of infection so as to surround it and then having dealt with it, are removed again and enabled to dispose of the injected bacteria. This mechanism is evidently upset by the injection of calcium salts and substances having a similar rupturing (of local defense) action. From the lesions in the bloodvessels and lymphatics indicating a stasis and the production of a clot of lymph and plasma it seems reasonable to conclude, that the disturbance of the vascular and lymphatic drainage of the tissues is responsible for the disturbance of the mechanism which presides over the movements of the leukocytes toward the focus of infection and away from it."

Observations on the Functional Activity of the Suprarenal Gland in Health and Disease.—The thesis which is supported in this paper by CRAMER (*Report of Imperial Cancer Research*, 1919, vi, 1) is that the thyroid and adrenal gland functioning together form an apparatus for the heat regulation of the body by means of their internal secretions. A study of heat regulation or heat production is not undertaken, but the author centers his attention upon the morphological changes in the adrenal and thyroid. The observations were largely carried out on mice which were subjected to cold, infection, acidosis, hemorrhage and anesthesia. Experimental hyperpyrexia was associated with congestion and partial disappearance of the colloid of the thyroid. The author describes a method for the histochemical demonstration of adrenalin within the cells of the suprarenal. Osmic acid precipitates fine granules within the cells of the medulla, which may be differentiated from fat droplets. These are spoken of as adrenalin. Lethal doses of tetrahydronaphthylamine and severe exposure to cold act as powerful stimuli to the adrenal with massive secretion. The medullary cells

discharge their adrenalin (which may be seen in the veins) and then undergo lysis. This massive discharge causes congestion of the lungs and hemorrhage. Moderate stimulation of the gland leads to an increased output without an unloading of the adrenalin contained in the medullary cells. Thus the condition of the adrenal in relation to its secretion is dependent upon the intensity of the stimulus. Somewhat similar results were obtained by infection. With a streptococcus of low virulency the suprarenal was found to be in a state of stimulation without depletion of its adrenalin, while more virulent strains and infection by the organisms of gas gangrene led to marked exhaustion of the gland both of its adrenalin content of the medulla and the lipoids of the cortex. The author found that the lipoids of the cortex played a part with the medulla in the formation of adrenalin. Following post-operative shock the suprarenal was not exhausted but its tissues were still loaded with adrenalin granules and were actively secreting these into the central vein at a time when there was low blood-pressure and a subnormal temperature. This finding is claimed to be in agreement with that of Stewart who showed that there was no alteration in the quantity of adrenalin in shock from that of a normal animal. The entire work of Cramer is based upon the morphological demonstration of the functional activity of the thyroid and adrenal. Many points will require the biological test.

The Cultivation of Recently Isolated and Laboratory Strains of Human Tubercle Bacilli on Artificial Media.—CORPER (*Am. Rev. Tbc.*, 1919, iii, 461) used for cultivation sixteen different media having a basic composition of salt, ammonium phosphate and agar. He grew human tubercle bacilli which had been artificially cultivated for about one year on this basic agar with the addition of glycerol and one of the following: defibrinated rabbit's blood, egg, ground up tissue, beef extract and peptone. Old laboratory strains six to eight years old did not grow on this basic agar with glycerol alone. Recently isolated human tubercle bacilli revealed a disposition of growing only upon a few media. They grew most constantly on the glycerol agar with the addition of egg or rabbit's blood. A few of the strains grew on all of the media on which the old cultures grew. Some of the delicate strains would not grow even when egg or rabbit's blood was added. With both the recently isolated and the old cultures there was a distinct difference in the growth ability of the different strains.

An Investigation of the Acid Fastness of Tubercle Bacilli.—EHRlich, Klein and Marmorek observed that young tubercle bacilli are not acid-fast. Marmorek suggested that this was due to their not having had time to develop the fatty waxy capsule which is supposed to be responsible for the resistance to decolorization. Wherry modified this acid fastness by growing the organism on media unsuitable for the synthesis of fats and the development of the capsule. SUYENAGA (*Am. Rev. Tbc.*, 1919, iii, 473) was unable to corroborate the observations of Ehrlich, Klein and Marmorek. He transplanted a saphrophytic strain of tubercle bacilli every two days from the transparent edge where the growth is younger. The medium used was glycerol agar 0.8 acid to phenolphthalein. This rapid transfer for 334 generations had little effect on

the acid fastness of the organism. Growth upon the non-nutrient and the "ameba media" used by Wherry in his work, considerably reduced the acid fastness but did not altogether destroy it. He also found that reactions of culture media, varying from 1.5 acidity to 2.0 per cent. alkalinity to phenolphthalein had little effect upon the acid fastness of the tubercle bacilli.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Prevention of Fatigue in Manufacturing Industries.—SPAETH (*Jour. of Industrial Hygiene*, 1920, vol. i, No. 9) states that the absence of a critical preliminary analysis has led to a confusion in the minds of certain physiologists between normal fatigue in industry ("industrial fatigue"), which is harmless, and cumulative fatigue, which is dangerous and may be associated with serious nervous disorders (industrial psychoneuroses). So far as we are aware there exists at present no valid quantitative physiological test for cumulative fatigue. Since normal fatigue may merge insensibly into cumulative fatigue, the reduction of normal fatigue to a minimum is the first logical step in a prophylactic attack. Normal fatigue may be reduced by a careful adaptation of all environmental factors such as illumination, ventilation, humidity, temperature, disposition of machinery, seating facilities, periods of rest, adequate and nutritious food, etc., to the physiological requirements of the workers. There is a great need for physical, physiological and psychological standardization of industrial workers by trades and processes. We have suggested a number of simple tests or types of tests that could be applied in a large variety of industries. Such tests are important for adolescents from fourteen to twenty years of age, as well as for men and women in industry. A number of physiological shortcomings of scientific management are discussed, especially the untrained type of time-study man and certain highly unscientific aspects of time and motion study methods.

Syphilis in Railroad Employees.—STOKES and BREHMER (*Jour. of Industrial Hygiene*, 1920, vol. i, No. 9) state that a general medical examination of 1763 patients of the Mayo Clinic showed 3.1 per cent. of them to have syphilitic infections obvious enough to be detected without the use of the routine Wassermann test. Four and two-tenths per cent. of the men and 2.6 per cent. of the women have

the disease. The lowness of these figures reflects, to some extent, the weakness of clinical judgment in the recognition of this disease as compared with current figures based on the routine Wassermann test. Part of the lowness of these figures is attributable to the large farming element in the clientele of the clinic and to the low incidence of venereal diseases in the States from which most of the patients are drawn. Of the railroad employees examined, 11.7 per cent. had syphilis. The disease was eight times as frequent in them as in farmers (1.5 per cent.), three times as frequent in them as in business men (3.8 per cent.), and twice as frequent as in laborers (6.1 per cent.). The doubtful value of the history of infection and the blood Wassermann test in the recognition of these cases is shown by the fact that 24 per cent. of the patients gave no history of infection other than gonorrhoea; 62.5 per cent. had observed no secondary manifestations and 53 per cent. were completely Wassermann-negative on the blood. On the other hand, 64 per cent. of those whose spinal fluids were examined showed positive findings. Of the diagnoses, 58.7 per cent. were contributed by laboratory procedures; 41.3 per cent. were identified by routine physical examination. Of the men examined, 79.5 per cent. had syphilis of the nervous system; 18.7 per cent. had cardiovascular syphilis. Pupillary abnormalities, muscular paralyses and fundus changes were present in 62.5 per cent. of the cases. Of the cases examined, 65.1 per cent. showed abnormal knee reflexes, and similarly high percentages prevailed for the other simpler details of the neurologic examination. Definite mental symptoms were present in 38.4 per cent. The above findings suggest that the routine railroad medical examination is insufficient to protect the public from the dangers of syphilis in men concerned in the operation of trains. Three suggestions are made with a view to increasing the efficiency of the railroad medical examination with respect to the recognition of syphilis: (1) Routine Wassermann tests should be performed on all employees between the ages of seventeen and twenty-five years, by a competent State board of health laboratory, and repeated on all employees reaching thirty-two years of age. (2) There should be annual effective examination of men between the ages of twenty-five and forty rather than of men over fifty years. Such examinations should include more attention to pupillary reactions than is at present given, and should employ those fundamentals of the neurologic examinations, such as tests of the deep reflexes, Romberg, etc. These can readily be performed by competent general examiners. (3) Formal educational propaganda should be undertaken by railroad medical departments for the education of medical examiners and employees alike to the great significance of syphilis in industrial insufficiency and personal ill-health.

The Prevention of Simple Goitre in Man. KIMBALL, ROGOFF and MARINE (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1873) report results on the prevention of goitre based on the examination of girls in the public schools of Akron, Ohio, in grades from the fifth to the twelfth, inclusive, made from November 26 to December 3, 1918—nineteen months after beginning the prophylactic use of iodine. The method used was to administer 2 grams sodium iodide in 0.2-gram doses for ten consecutive school days, repeated each autumn and

spring. The results showed that simple goitre may be prevented on a large scale and that the method is practical and economical and can be recommended as a public health measure in goitre districts. The danger of iodism or of exophthalmic goitre from such amounts of iodine as were given is shown to be negligible.

Complement Fixation in Diagnosis of Tuberculosis.—MOURSUND (*Jour. Infect. Dis.*, 1920, xxvi, 85) states that the complement-fixation test for tuberculosis as described in his article is of no value as a diagnostic or prognostic aid. The complement-fixation test for tuberculosis with alcoholic extract of tubercle bacilli as antigen, is not specific. Not all complement-fixation tests with bacterial antigens are specific. A large percentage of serums giving a positive Wassermann give fixation with tubercle and gonococcus antigens. A certain number of individuals not infected with tuberculosis or gonorrhoea will give positive fixation tests with one or both of the corresponding antigens.

The Fate of Bacteria Introduced into the Upper Air Passages.—BLOOMFIELD (*Am. Rev. Tuberculosis*, 1919, iii, 553) states that the general result of his experiments indicates that even after a short period of time it is usually impossible to recover *sarcina lutea* swabbed in large amounts on the tongue, nasal mucosa, or into the crypts of the tonsils. Whereas, disappearance from the nose was somewhat slower than from the other sites, in only one case could any organisms be recovered after twenty-four hours, and in none after two days. Cultures made in this way do not, of course, prove the complete absence of the microorganism in the mouth and nose, but the general trend of the quantitative relations indicates a rapid disappearance. The fact that the estimated dose of 50 to 100 billion organisms was vastly greater than that in any natural infection, indicates the remarkable efficiency of the mechanism present in the upper air passages for disposing of this organism. An analysis of the possible factors active in effecting this disposal indicated that retraction of mouth secretions, mechanical action and other mouth bacteria play little, if any part, but the saliva and mouth secretions exert a prompt and marked bactericidal effect. Similar methods are being used in studying the fate of other microorganisms introduced into the upper air passages.

Potency of Antimeningococcal and Antipneumococcal Serums.—The measure of control enforced at the Hygienic Laboratory of the U. S. Public Health Service (*Public Health Reports*, 1919, xxxiv, 2657) with respect to the serums used in the treatment of pneumonia and meningitis are described in great detail. In each case it is required that the serum under test shall compare favorably with the standard. In the case of the antipneumococcus serum a mouse-protection test is employed, while serological methods are depended on for evaluating the antimeningococcus serum.

Closing Schools as a Means of Controlling Epidemics.—Committees of the United States Bureau of Education and of the American Public Health Association (*Public Health Reports*, 1919, xxxiv, 2668)

as the result of an investigation report that the successful control of epidemic disease among school children requires: (1) Keeping the schools open, with the possible exception of sparsely-settled rural districts when medical inspection cannot be obtained and where aggregation takes place only in the schools. (2) Careful daily or frequent periodical inspection of schools. (3) Careful provision for exclusion of cases and contacts, emphasis being placed on clinical data rather than upon fixed periods of exclusion. (4) Systematic home visitation. (5) Reliance upon natural and physical cleansing rather than upon chemical disinfectants.

Steam as a Bedbug Eradicator.—The Public Health Service (*Public Health Reports*, 1919, xxxiv, 2713) describes the destruction of bedbugs in a large bunk-house in which it was possible to subject the whole interior of the building to steam. A temperature of 160° F. maintained for three hours was found to be effective. The building was still free from bugs two months after the steaming.

Botulism from Eating Canned Ripe Olives.—ARMSTRONG and STORY (*Public Health Reports*, 1919, xxxiv, 2877) report an outbreak of 14 cases of botulism from the eating of ripe olives. Seven of the cases proved fatal. The circumstances of the outbreak were such as to render study by epidemiological methods very easy. Such methods point directly to the olives as the source of the poisoning, and an examination of some of the suspected material showed it to contain the toxin of the *Bacillus botulinus*. The olives in question were remarked to be of abnormal taste, and closer examination showed that they were certainly spoiled. Only three persons among the seventeen who ate of the spoiled olives failed to develop clear indications of botulism. Under the section on prevention the author states that: (1) The epidemiological investigation points to the ripe olives as the vehicle of the poison. (2) The olives and brine were found to be highly toxic for animals, both when fed and when injected. (3) The organism isolated from the olives and brine seems, from its morphology, cultural characteristics, toxin formation, and from the symptoms and pathological lesions produced, to be a strain of *Bacillus botulinus*. (4) Antitoxin and agglutinins could not be demonstrated in the blood of recovering patients forty-five days after the dinner. (5) Alcohol has the property of neutralizing the toxin when mixed *in vitro*. (6) It would seem that *Bacillus botulinus* does not produce its toxin under usual conditions in a warm-blooded animal.

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ORIGINAL ARTICLES.

SIR WILLIAM OSLER AS A MAN OF LETTERS.¹

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THERE are men of talent who do the one work in life they are peculiarly fitted for and nothing more. In all else they are like us ordinary mortals. There are others for whom work along one line, of one kind, is not enough. They have such wide interests, such capacity for intellectual labor, such a large mental outlook, live in such a rich intellectual world, that they are compelled to do serious work in several fields. Others can do one kind of important work well, but must also have some other intellectual pleasure. Such men seek avocations as well as vocations. An avocation is a glorified hobby. Just as small souls collect postage stamps, or play chess, or golf, or do some other harmless thing, so certain greater souls must rest their minds, not by idleness and sleep as does the dog, or by impish play like our distant cousin the monkey, but by some pleasant and, at the same time, useful productive work. The pursuit of letters is such an avocation, and one that appealed strongly to Sir William Osler as it has appealed to so many physicians. I say has appealed, because there is a justified fear that the newer methods of education which certain philosophers of the meaner sort are trying to force on the coming generation and our worship of specialism, not

¹ Read at the Osler Memorial Meeting, College of Physicians of Philadelphia, March 3, 1920.

only in medicine, but in all kinds of work, will end in breeding men who will have little interest in, or pleasure from, pure scholarship for its own sake. The movement is not a permanent one but will do much injury for many years. Osler was out of sympathy with any such method of improving the race; he belonged to a world that is dead or rather in eclipse. He, as a boy, lived in an old-fashioned, intellectual atmosphere; his mind was fed not on mental pap but on real literature. His early taste was not spoiled by the worthless stuff sent out by the printing presses of today, in such huge quantities that real literature is smothered. In his boyhood the making of books was expensive: wood pulp and multiplex printing presses were not yet invented. The book trade catered to the full-grown intellect. Much that was printed was dull, stupid and soon found its proper place, but much was scholarly, and, not a little, good, strong meat for full-grown men. The paranoiac, whom we have always with us, had to have a well-lined pocket-book to get his crazy panaceas for social and political evils printed. He was not welcomed in the Sunday supplement and the uplift magazines because they had not been imposed on a much suffering people. The Bible was still a living book; the subjunctive mood had not gone out of existence; sentences did not have to be reduced to the length of a clause, lest the reader should have brain-fag, and colons and semi-colons were still in common use. Punctuation was a well-known art. People either read or did not read, and if they read they read and studied things worth the reading. They did not disdain to reread and got on friendly, or it might be very unfriendly terms with an author, but they at least knew his works.

More important, he belonged to a generation which followed the old tradition, that the physician ought to be a scholar, first broken away from by Germany and, later, following Germany's example, by us. Today we have wandered far from tradition, and under the pernicious influence of so-called efficiency are trying the experiment of vocational training. Theoretical pedagogues of the newer school, pretending they have discovered a new psychology, teach us that to be efficient the boy must, from a very early time, learn only the things useful in his future work. The disciples of efficiency do not realize that the one thing we need is well-grown, well-rounded-out men. Osler grew up in an atmosphere of real efficiency, an atmosphere which made men able to get all out of life that life has to give, and hence able to give back abundantly.

Environment reinforced his strong hereditary bent toward appreciation of letters and, in addition to appreciation, he had the impulse to accomplish. The two do not always go together: ability to enjoy is much more common than ability to create. Indeed, sometimes among men whose trade is writing there is a curious lack of appreciation, of power to appreciate, at least the work of others. But this is a human failing having deep-seated causes. Writing with

him was not a trade, not a thing done for money or fame, but for very joy in the doing, his pleasure, his rest from serious work. Another motive was that he realized well his peculiarly powerful personal influence on students, and, as he firmly felt the need of scholarship in physicians, in order that they should have such a grasp on all culture that they would see nature as a whole, and see the real relations between things which to the vulgar mind seem to have nothing in common, he strove in his non-medical essays to stimulate an appetite for the study of biography and history, the keys which open the lock of philosophy. He handed on the torch to sympathetic hands; that was easy enough; but more than that, he made kinetic, potential tendencies in many a young man who might otherwise never have been stimulated in the right way. He knew full well that to understand the medicine of today one must know the medicine of the past, and many of his essays deal with that subject. He was consciously or unconsciously ever fighting the pernicious German intellectual influence in medicine which has done so much harm in America. I mean the idea that advance comes from each man taking up some one little subject and studying that thoroughly. Now there is good in this, just as there is good in a method of modern industrial life whereby a man in, say shoemaking, is taught to do some one little thing until he becomes almost as automatic as the machine itself. The good is that shoes are cheaper, more people can therefore buy them than in the old days; the evil is the shoemaker is not a man but a cog. Further, no such workman will be able to see shoes in relation to the universe and invent some better foot-covering. So in medicine the research workers by the German system rarely make great discoveries, and as men they will insofar be failures in that they will not get all that is possible out of life. One reason why modern Germany has made relatively so few great fundamental discoveries in science, why it has had so few stars of the first magnitude, while having made so many little discoveries, having so many minor stars, is this very thing, that the Germans have carried specialism so far that each man's mental life is passed in a world too small for him to see the great universe.

Wide as were Osler's intellectual interests, many of his friends were astonished at his acceptance of the invitation to deliver the Ingersoll lecture on "The Immortality of Man." He declined once, but when a second invitation came he felt he could not again refuse, the more especially because President Eliot told him others of his profession had also declined. The inference seems to be that a refusal to lecture on the subject might strengthen the popular opinion that where there are four physicians there are three atheists. There is no need to say that Osler's philosophy did not agree with the saying. In a private letter to a friend he classed himself as a subconscious Teresian. What that is everybody who has studied the history of religion knows, and those who have not manifest a

lack of interest in the matter of which they need not be proud. He chose for his title "Science and Immortality." In the lecture he frankly confesses science cannot help in deciding the question as to whether there is personal survival after death, points out that whole races have played their part and come and gone and been careless of immortality, that even today, though a small number of people live this life as a preparation for the life to come, the majority are in no way influenced in conduct or in thought by what the future may be. His own feeling is that "to keep his mind sweet the modern scientific man should be saturated with the Bible and Plato, with Homer, Shakespeare and Milton: to see life through their eyes may enable him to strike a balance between the rational and the emotional, which is the most serious difficulty of the intellectual life." This is good advice, but whether it is followed will depend primarily on a man's protoplasmic make-up and in less degree on his childhood's nurture. Intellectual affinity is quite as real as chemical, nor more nor less mysterious, and how Smith or Jones or Robinson will react to Plato or Milton or any other mind, whether there will be any reaction, or if any what, depends on things we know nothing of and certainly have no control over.

Osler showed his zest for letters and his ability therein even in his purely medical writing. This is nowhere better shown than in his paper on "The Treatment of Disease," written for the *The Oxford Medicine*. Written when he was no longer young, I think it was among the last things he did, it is his apologia for his therapeutic methods. You all know, of course, that the therapeutically erudulous, the lovers of every new drug, the worshippers at the shrine of the idol medication, called him a therapeutic nihilist, and not always in language to be used by tongues polite. They have not, and will not, enjoy this essay, especially as there is an undertone running through the whole indicating that polypharmacists may not know quite as much as they imagine. His emphasis on the fact that the starting-point of all treatment is a thorough knowledge of the natural history of disease is not pleasant reading to the gentlemen who much prefer to spin cobwebs of therapeutic method, out of a thread of dream physiology, spun with busy pens on paper at a writing desk.

Most of Osler's essays had some relation to medicine. He was from early manhood particularly interested in biography. One whole volume entitled *An Alabama Student and Other Biographic Essays* contains only biography. But he was interested in these men not only as physicians but as men, and especially as men who conquered obstacles; men who by sheer effort of mind had done things and thought things others better placed, sometimes, had neither done nor thought. His social instinct was so great that he was not content to have many living friends scattered over the whole world, but was compelled to hunt up all the dead worthies

who had done things and been forgotten. In friendship he resurrected them that they might have more friends.

He was strongly influenced by Greek thought. He was so profoundly Platonic that more than once in writing, and many, many times in common talk, he said he would rather be wrong with Plato than right with anybody else. His worship of Greek philosophy pervaded him: it influenced him in many ways: even in his strictly scientific writing now and again a reference to Plato appears. As I know no Latin and less Greek, and can make no claim to any deep knowledge even of Jowett, but am a sort of barbarian (in the older sense) who has read a little philosophy, mainly to be astonished to find how modern, how familiar much of it seems, I am entirely incompetent to speak on matters with which Osler was familiar. I am somewhat like the woman who was astonished at the number of quotations Shakespeare used in Hamlet. I can only say that it might be useful to the world-rescuers of the newest school, who, as I understand, would abolish the study of history, since our problems are all new, and the study of ancient philosophy and science because those old thinkers are behind the times, to read, learn and inwardly digest what Plato has to say about education and not a few other things. I am sure if they have as open minds as they boast of having they would come away from such reading with a feeling of humility such as they have never had before. A few of them might even stop teaching in order to learn something themselves. Osler's interest in Plato and things platonic led to an honor which I think had never come to any other physician, the presidency of the Classical Association, at the meeting of which in May, 1919, he delivered the presidential address. His subject was "The Old Humanities and the New Science." The address is characteristic. It shows here and there his sly and sometime impish wit, his unexpected references to out-of-the-way characters in books, once popular but now forgotten, or reigning among the immortals in name only, having ghostly immortality, and finally his wisdom. He holds the balance true between science and the humanities and maintains what will ever be true, that the educated man needs both or he is not an educated man. The circumstances of the writing of this address impressed me tremendously. Written at an age later than that at which most men cease to think, and, if surviving in this world, are often in a sense mere automata, living in an intellectual past, the gates of the brain tight shut against the entrance of any new idea, no matter how strong the battle without and how great an effort is made to compel entrance, with emotions deadened, not, as the poets say, by increased wisdom but because the life-carrying stream passes more sluggishly over the cells which, in some mysterious way, secrete thought and bathes them in a fluid less rich in the hormones carried from distant organs, and because the sewers of the body are clogged, it shows no sign of age. Remember, too, its author had

lived through four long years of war, had seen his country wracked and driven almost beyond endurance, and finally had suffered the sacrifice of his only son and child. The man who could endure all this and yet make such an address needs no argument to prove his worth.

Osler made no pretense to being a great light in literature; none of his essays will give him a living immortality; they will of necessity soon be put on the upper shelves in the store rooms of libraries and only be read by medical antiquarians hunting up the lives of old worthies, just as he shook the dust from many an old volume written by men one time great and resurrected only because he had a mind curious to know the steps that led to the growth of science and of medicine. But the influence his essays have had on the men of the days of his teaching will be a never-dying force for good. Just as there is an immortality of matter carried from generation to generation, so there is an immortality of thought passed on from teacher to student. Few men have chosen their hobbies so wisely as he. He helped others in getting his own greatest pleasures.

SIR WILLIAM OSLER AS HOST TO AMERICANS IN ENGLAND DURING THE WAR.¹

By GEORGE WILLIAM NORRIS, A.B., M.D.,

PHILADELPHIA

IN the autumn of 1904 a young man recently emerged from a hospital internship, and having had the temerity to send out certain medical reprints, received the following letter:

"Thanks for your papers, with which I am greatly pleased, not only for the evidence of good work they show, but for the memory of your father and grandfather. The tuberculous endocarditis paper is most interesting and will be useful, as I have just been going over all our material on the subject. Could you not come down this winter and give us a little talk at our Laennec Society? I send you a program and you will see the sort of work we are trying to do."

Needless to say the young man accepted, and thus first tasted Oslerian hospitality and fell under the spell of Oslerian influence.

The incident itself is of interest only in that it exemplifies what was happening to other young physicians in other cities. The mere fact that someone did read reprints, and especially that no less a man than Osler himself had shown a personal interest in one's

¹ Read at the Osler Memorial Meeting, College of Physicians, of Philadelphia, March 3, 1920.

efforts, was a stimulus as effective as it was widespread. Is it any wonder that Osler's death is so strongly felt as a *personal* loss by so large a part of our medical profession. And is it any wonder, on the other hand, that Osler could do and did so much during the great war in having the young Americans and Canadians who went to England assigned to duties and positions best suited to their abilities?



Sir William at Oxford during the War.

In May, 1917, when the first American Base Hospitals arrived in England, among the first to meet them and extend a welcoming hand was Sir William, who seemed to be everywhere: handshaking with everyone and inviting many to his home. During the year ending last summer alone no less than sixteen hundred guests broke bread at his table. From our first entrance into the war until long thereafter a constant and steady stream of Americans flowed to Oxford. From hundreds one heard in France of their delightful welcome there.

Nor must we think that such hospitality was extended only to

friends and persons of distinction. There were probably no men in the whole American service so lonely, lost and forgotten as that lot of unattached medical officers, upward of one thousand in number, who were sent overseas in the early days attached to British battalions, and as reward for their prompt patriotism, denied consideration as well as promotion by our War Department. Many of these men were welcomed at Oxford, although for the most part they were entire strangers to Sir William by both name and reputation.

Those who again visited Sir William after the Armistice, after the death of his son, were amazed to see with what an unconquerable spirit he met his awful loss. There was the same self-effacing kindness and sacrifice, the same hospitality and farewell dinners even for those about to return home—dinners graced by men of international repute, because Sir William was the host.

Of the hospitality meted out at 13 Norham Gardens it is difficult to speak. One did not have to be told one was welcome—one somehow felt it. It was indeed a place where, as related in the old Norse Saga of Frithiof, "Hospitality sat in gladness." She strained not, but pervaded all things. Whether one wandered in the gardens with Lady Osler, who wistfully showed one her pet flower-beds ploughed up to grow potatoes; whether one visited the military hospital or dined at old Christ Church College with Sir William; or whether of an evening one sat at ease before the open fire in the library, while being shown the treasured tomes that Osler knew and loved so well, it mattered not. The evenings passed quickly amid reminiscence, anecdote, flashes of wit and twinkles from those deep-set eyes; while questions were asked about those at home whom he had long not seen.

Advice and assistance were yours for the asking. Often indeed one heard: "You must see such and such a hospital; I will give you a letter." "Don't fail to visit ——; a splendid fellow; tell him I sent you." "If you want anything when in France drop me a line." "I was interested in your article on so and so and shall refer to it in my next edition." "You must read X, published in 1640; he was quite wonderful. But little of real importance has been added since."

Charming, always interesting and interested; always giving in full measure of himself and of his time; always brave and smiling, and with an only son in France in the heavy artillery. A son so much beloved that it is with much hesitancy and only in profound reverence I speak of an almost sacred incident.

It was long past bedtime; we were about to "turn in" and had lit our bed-room candles, when the cheery, well-known voice from the hallway called us back. "Do you mind? I should like to show you Revere's room?"

There it was, untenanted, but just as its occupant had left it. "You must see some of his books. Are not these gems? These old

editions of English classics which he has picked up. I hear from him every week."

The quiet room, in the sleepy town, the flickering candles, the musty volumes, the devoted father—it was a picture seen through an atmosphere of the teeth-gritting tenseness which pervaded the whole of England at that time; and with a background of that Hell that was being enacted across the Channel—a picture that will not be forgotten.

And it was not long afterward we learned that the dreaded blow had fallen, and that Revere, too, now slept in "Flanders Fields!"

THE DIAGNOSTIC SIGNIFICANCE OF INSPIRATORY MOVEMENTS OF THE COSTAL MARGINS.

BY C. F. HOOVER,
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SIX years ago the writer published an article¹ on the functions of the diaphragm and their diagnostic significance. In that article former interpretations of phrenic action were criticized and the relation between the curve of the phrenic plane and movement of the costal margins to which it is attached was discussed; experimental and clinical evidence was also presented, to show that inspiratory widening of the subcostal angle and the outward movements of the costal border are not expressions of phrenic excursion but that they are expressions of intercostal activation. It was also shown in this article that when the curve of the phrenic plane is flattened the diaphragm gains the mastery of the costal margin, and that when this is the case the costal margins move toward the median line during inspiration; and, furthermore, that inspiratory narrowing of the subcostal angle is not an evidence of phrenic excursion but purely an evidence of phrenic activation. The only agent which causes widening of the subcostal angle during inspiration is the intercostal musculature.

Four years later² the role of the scaleni, intercostals and diaphragm was discussed and the work of Duchenne and several of his contemporaries was reviewed. In this publication it was shown how Duchenne's results came to differ from the results of his contemporaries in performing the same experiment. Further evidence was adduced to show that the costal border phenomena depend entirely upon the plane of the diaphragm, and that when the plane of the diaphragm is convex on its under surface the costal margins

¹ Arch. Int. Med., 1913, xii, 214-224.

² Ibid., xx, 701-715.

move outward during inspiration, just as when the diaphragm is convex on its upper surface.

The results of the writer's former observations indicate that the direction and extent of inspiratory movement of the costal margins may be modified by the curve of the phrenic plane, by synechia between the diaphragm and the thoracic wall and by the nerve supply to the intercostal muscles and the diaphragm. These respiratory phenomena are not presented to the examining physician with a surface announcement of the underlying pathology. All that is visible to the examiner is the extent and direction of movement of the outer and inner parts of each costal margin, the movements of the arcs of the ribs and the protrusion of the epigastrium.

A direct method of discussing the role of the diaphragm is to consider the variety of movements of the costal margin during inspiration, and in this article I propose serially to consider the varying movements of these borders.

EXAGGERATED SYMMETRICAL OUTWARD MOVEMENTS OF BOTH COSTAL MARGINS. Such movements are seen in paralysis of the entire diaphragm, as from poliomyelitis. I have seen one such instance in a child, an account of which was published in the first article referred to. There was great exaggeration of the spreading of the hypochondria, and all of the costal margin of each side moved in an outward direction to an exaggerated degree. Another instance of complete paralysis of the diaphragm was seen in the terminal stages of spinal-cord disease in a woman, aged forty years, who had primary anemia. The exaggeration of the outward movement was due in both these cases to the loss of resistance to the widening movement of the costal margin, which is supplied by a normally acting diaphragm. Under such circumstances there is no opposition to the normal action of the intercostal muscles. Furthermore, the loss of phrenic action demands increased activity of the intercostals to compensate for the loss of phrenic descent during inspiration.

Two other cases were described in which there was exaggerated symmetrical spreading of the subcostal angle, with an exaggerated spread of the hypochondria. In one of these cases the curious movement was due to paralysis of the scaleni in a child with congenital myotonia. All the intercostals and the diaphragm were normal, but, owing to the want of normal anchorage from the scaleni there was an inspiratory retraction of the upper three ribs and manubrium,³ and the exaggerated outward movement of the costal margins and the hypochondria in this case was a compensatory measure on account of diminution of volume of the upper lung, which occurred during inspiration. This mechanism caused rebreathing between the upper and lower lung, so that the increased spread of the hypo-

³ Jour. Am. Med. Assn., 1919, lxxiii, 17-20.

chondria and widening of the subcostal angle constituted a purely compensatory measure, which was demanded by the mechanism of rebreathing.

Another patient had the same phenomenon of rebreathing between the upper and lower lung to such an exaggerated degree that it imposed on several medical men as a case of tracheal stenosis. This patient had normally functioning scalene muscles, but had paralysis of the upper four intercostal muscles of both sides. This vicious cycle of rebreathing was intensified just as the respiratory function was called upon for increased movements by exercise or by laughing and crying.

THE ENTIRE COSTAL MARGINS OF BOTH SIDES MOVE SYMMETRICALLY TOWARD THE MEDIAN LINE. This movement is observed (1) in patients who have paralysis of the intercostal muscles and in all instances of injury to the spinal cord in the cervical or upper dorsal region; and (2) in flattening of the diaphragm, due either to chronic emphysema or acute emphysema from bronchiolar spasm. This phenomenon enables us to estimate the degree of flattening of the phrenic leaf. It is invariably present in general bronchiolar spasm and is of service in differentiating between pseudo-asthma and genuine bronchiolar spasm, which occur in patients with chronic bronchitis and emphysema. Many of these patients have attacks which they interpret as genuine asthmatic attacks, when in reality the whole procedure is born of an asthmaphobia. These patients live in constant fear of an asthmatic attack and are liable to have much respiratory discomfort which is psychic in origin. In fact the only manner in which an accurate differentiation can be made between pseudo-asthma and genuine asthma is to observe the costal margins. If the costal margins do not move toward the median line during inspiration then the observer may be perfectly sure there is no bronchiolar spasm, for with bronchiolar spasm there is always sufficient increase of total volume of the lung to flatten the diaphragm sufficiently to procure its mastery over the costal margins.

In the absence of bronchiolar spasm this sign is of great service in estimating the severity of chronic emphysema. When a patient suffering from chronic emphysema, attended with bronchitis, has sufficient enlargement of his lung to give him cyanosis, with a carbon-dioxide percentage in the alveolar air of 7 per cent. or more, there is invariably a sufficient flattening of the entire diaphragm to cause inspiratory narrowing of the subcostal angle and inspiratory retraction of the entire costal margin of both sides. Percussion fails to give us accurate information on this point, because from percussion we can learn only about the descent of the edges of the lung into the pleural sinus, and the pleural sinuses may be completely filled with emphysematous lung and still the entire body of the diaphragm will not be sufficiently flattened to cause inspiratory retraction of the costal margins.

The significance of respiratory retraction of both costal margins was demonstrated in a patient who on entering the hospital breathed fourteen times a minute and had seven liters of tidal air per minute. The patient was cyanotic. The dyspnea and air hunger were very pronounced. The patient's alveolar air, as estimated by the Haldane method, contained 7.3 per cent. of carbon dioxide. This patient had a chronic bronchitis and emphysema, and at the same time did not seem to have bronchiolar spasm. His real difficulty was apparently due to hyperemia of the mucosa of his bronchial path, although this was not proved at the time by the employment of adrenalin or any other drug to show there was no bronchiolar spasm. After two days the patient no longer suffered from air hunger or dyspnea and the cyanosis had disappeared. The patient's alveolar air contained 5.3 per cent. of carbon dioxide instead of 7.3 per cent., as at the time of entrance, but he was still breathing fourteen times a minute, and breathed seven liters of air just as he did at the time of entrance. The difference, however, between the two periods was that on entrance the patient was suffering from intense air hunger and was employing all his strength to ventilate his lung fourteen times a minute, with a half-liter of tidal air at each respiration. In the latter period he breathed at the same rate, with the same tidal air, in perfect comfort. So when this man was at rest he required a seven-liter minute volume of air to properly ventilate his lungs. Now, with the added work which was thrown upon him with stenosis of his bronchioles he demanded, of course, an increase in oxygen consumption, and should have required, as a consequence, a minute volume of air which was beyond his ability to breathe.

This was not the only difficulty with this man. In the first period he had an emphysema which was much severer than during the second period. This, however, was not demonstrable by percussion because at both periods the lower borders of the lung filled the pleural sinus. At the time of entrance to the hospital, however, both costal margins in their entire extent were drawn toward the median line during inspiration; and in the second period, when he was no longer cyanotic, was not suffering from air hunger, and the carbon-dioxide percentage in the alveolar air had diminished 2 per cent., the costal margins were no longer drawn toward the median line during inspiration, but either remained constant in their relation to the median line or showed slightly lateral movements. The movement of the costal borders was the only physical sign on which one could have diagnosed a higher grade of emphysema during the period of dyspnea and cyanosis.

THE ENTIRE COSTAL MARGIN OF ONE SIDE MOVES FARTHER AND MORE PROMPTLY IN AN OUTWARD DIRECTION THAN THE OTHER BORDER. In observing the costal margin of course one must also take into consideration the movement of the entire arc of the ribs, but when the arcs of the ribs on the two sides move symmetrically,

but the costal margin moves farther on one side, it indicates there has been some accentuation of the arch of the diaphragm on the affected side. This disparity of movement is seen in acute diseases of the liver. On several occasions the writer has observed an increase in the lateral movement of the costal margin of the right side when the patient had an acute swelling of the liver due to parenchymatous disease. This was apparent when the liver did not extend below the costal margin. However, the increase in the outward movement of the margin of the right side indicated there was a greater increase in the volume of liver than the position of its lower border indicated. As these patients recovered from their acute hepatic swelling the costal margins again resumed a perfectly symmetrical movement.

This phenomenon is also seen in subphrenic abscess. The first patient of this kind the writer observed was a man who had had gallstones, was operated, returned home with what seemed a satisfactory convalescence, and reentered the hospital two months afterward with fever and air hunger. The entire right thorax was flat on percussion from the clavicle to the costal margin. There was a large subphrenic abscess which had ruptured into the pleural cavity, and the liver was displaced nearly a hand's breadth below the costal margin. In spite of total want of pulmonary ventilation on the right side the right costal margin moved laterally much farther than the costal margin of the left side, where there was no disease of the lung or pleura. This exaggerated outward movement of the costal margin on the affected side suggested an impairment of the diaphragmatic influence on the movement of the costal margin, either because the arch of the diaphragm on that side was greatly accentuated by the subphrenic abscess or because of a myositis of the muscular leaf of the right side.

Since this experience the writer has known of five cases of subphrenic abscess, all of which were attended with dulness on percussion, impaired tactile fremitus and bronchial breathing over the base of the right thorax. In all of these cases the diagnosis of subphrenic abscess was made solely on the fact that the costal margin of the affected side moved farther away from the median line than did the costal margin on the healthy side. However, in the course of the formation of a subphrenic abscess, should the diaphragm be displaced in an upward direction, the pleural sinus obliterated, and synechia between the diaphragm and the thoracic wall take place, then a new point of attachment would be formed, so that the effective part of the diaphragm on the right side, namely, that portion which extends from the central tendon to the point of synechia, would have a flattened plane on its upper surface, and instead of the costal margin moving farther away from the median line during inspiration it would move toward the median line. This actually occurred in one case of subphrenic abscess which recently came to operation on

the surgical side of Lakeside Hospital. The costal margin of the right side moved toward the median line during inspiration. A differentiation of thoracic empyema was made as against subphrenic abscess, but at operation a subphrenic abscess was discovered. So far as could be learned at operation the diaphragm was fixed to the thoracic wall, and it was evidently this fixation which gave the misleading sign.

The only suprathrenic or intrathoracic disease which thus far has been observed to give an increased outward movement of the costal margin of the affected side is massive collapse of the lungs. In massive collapse of the lungs we have an acute shrinkage of a large portion of lung without preliminary disease of the affected lung. It has been frequently observed to occur in the lower lobe of each side; and when the lower lobe or both lobes of one side are involved, diminution in volume of the lung is unaccompanied by synechia between the lung and the chest wall or between the chest wall and the diaphragm. This is a rare occurrence and it was little observed prior to the war. With massive collapse of the lower lobe or the entire lung of one side the diaphragm is greatly increased on its upper surface, and although during inspiration there may be no lessening of the vigor of activation of the diaphragm on the affected side, its influence on the movement of the costal margin will have been lessened, and consequently, with lessening traction of the diaphragm on the costal margin, its outward movement will be accentuated.

This is a very valuable diagnostic point in diagnosis of massive collapse of the base of the lung. With massive collapse of the base there will be marked dullness and high-pitched bronchial breathing, with an increased outward movement of the costal margin of the affected side. The differential diagnosis will, of course, lie between subphrenic abscess and collapse of the lung, but in collapse of the lung one can make out other evidences of diminished volume of the affected lung. Not only will the diaphragm be displaced in an upward direction, but the heart and mediastinum will also be displaced toward the affected side. In cases of chronic fibroid disease of the lungs we usually have synechia between the diaphragm and the chest wall. The lung is diminished in volume and increased in density, and there is fixation of the leaf of the diaphragm to the thoracic wall. Here we have not only an upward displacement, but also an upward fixation of the diaphragm, and for this reason chronic fibroid disease of the lung is accompanied by diminished excursion of the costal margin or the costal margin is moved toward the median line during inspiration. Should fibrosis and contraction of the base of the lung be unaccompanied by obliteration of the pleural sinus or synechia between the diaphragm and the chest wall, then, of course, we would have exactly the same physical signs that occur in massive collapse. Wherever this question of differential diagnosis

occurs we have, of course, the previous history to guide us in the differentiation. So thus far collapse of the lower lobe of the lung is the only condition in which the costal margin acquires an increased outward movement during inspiration. Captain M. A. Blankenhorn, of the A. E. F. in France, had ample opportunity to make this observation, and he assures me that the increased outward movement of the costal margin on the affected side was one of the most striking and helpful diagnostic points in making the diagnosis. The essential physical condition for bringing about this unilateral increased movement of the costal margin is a diminution in volume of the lower lobe of the lung unaccompanied by synechia between the diaphragm and the chest wall.

THE COSTAL MARGIN OF ONE SIDE MOVES TOWARD THE MEDIAN LINE. When the costal margin of one side moves toward the median line during inspiration and the other side moves in an outward direction it means that the diaphragm on the affected side has gained the mastery of the costal margin. This will occur when the diaphragm is sufficiently depressed or when the intercostal muscles of the same side are paralyzed. When the dominance of the diaphragm is due to paresis of the intercostals of one side on account of spinal cord disease, there is, of course, no evidence of intrathoracic disease, and not only the ends of the affected rib move toward the median line during inspiration, but the entire arc of the rib will fail to move or will be retracted during inspiration. Unilateral retraction of a costal margin, that is, an entire unilateral movement toward the median line during inspiration, is not a pathognomonic sign of pneumothorax or pleurisy with effusion. It is merely an evidence of the lessening of the normal curve of the phrenic leaf. It does not matter whether the diaphragm is convex on its upper or on its lower surface. In either case the phrenic control of the costal margin is lost. And what is still more significant, it does not matter whether the phrenic leaf of the affected side moves upward or downward during the inspiratory act; the costal margin will move away from the median line if there is sufficient curve to the diaphragm to lose the mastery of the costal margin. This is seen in large effusions into the pleural cavity and also in pneumothorax when the contained air has a pressure above that of barometric pressure. An instance of right-sided pneumothorax, with positive pressure in the pleural cavity and concavity of the upper surface of the diaphragm, was very plainly visible under the fluoroscope. During inspiration the diaphragm on the right moved upward and on the left moved downward. The costal margins on both sides moved away from the median line, but on the right side there was lessened movement in an outward direction. The liver moved upward during inspiration. When the air-pressure was released by paracentesis so that barometric pressure prevailed in the pleural cavity, there was no excursion of the diaphragm during inspiration, but the costal margin of the right side moved strongly toward the median line.

In three instances of large accumulation of fluid in the pleural cavity the spleen was displaced well below the costal margin, the whole left thorax was flat to percussion and tactile fremitus was absent, the respiratory sounds had a bronchial character and there was marked whispered pectoriloquy. The costal margin of the left side moved in an outward direction, but much less than on the right side. With a large accumulation of pus in the pleural cavity one could not see the plane of the diaphragm as in the case of pneumothorax. However, owing to the fact that the entire pleural cavity showed evidences of effusion, paracentesis was performed and two pints of fluid were removed from the pleural cavity. Then the costal margin of the affected side was seen to move strongly toward the median line during inspiration. The pleural cavity was aspirated as completely as possible and the costal margin again moved in an outward direction, although it did not move as far as the costal margin of the opposite side.

These experiences prove two very important points: One is that the direction in which the costal margin will move does not depend upon the position of the diaphragm but on the curve of its plane. The result is quite the same whether the convexity is on the upper or lower surface. These experiences also prove that the outward movement of the costal margin of the affected side does not depend on the descent of the viscera during inspiration. As was seen in the case of pneumothorax, when the liver moved upward during inspiration the movement of the right costal margin was away from the median line.

All these signs may sometimes fail us in making a diagnosis. For instance a woman recently under my observation had a subphrenic abscess of the left side, with fetid empyema, attended with the evolution of gas in the pleural cavity. The patient had all the signs of pyopneumothorax and the costal margin of the affected side moved outward during inspiration. An operative procedure was undertaken; the eighth rib was resected in the axillary line, fetid pus in large amounts was evacuated and a marked convexity of the diaphragm could be clearly seen. Paracentesis through the diaphragm revealed a large subphrenic abscess. Now, in this instance we had a combination of subphrenic abscess with pyopneumothorax of the same side. The position of the diaphragm, so far as we could determine, was pretty nearly that of the normal arch; so the loss of movement of the costal margin on the affected side was due entirely to the want of ventilation of the lungs and the consequently impaired movement of the ribs in their entire extent, but what movement of the costal margin was apparent was in an outward direction.

UNILATERAL BRONCHIOLAR SPASM. A patient with chronic bronchitis and emphysema and frequently recurring attacks of bronchiolar spasms had an attack of asthma in which the costal margin of the left side moved toward the median line, but the right

costal margin moved outward. The patient was given adrenalin, as on many former occasions, and its administration was followed by prompt relief of the asthma; directly the bronchiolar spasm ceased there was symmetrical outward movement of both costal margins. Unilateral bronchiolar spasm is a very unusual clinical experience, but this man gave us several exhibitions of this phenomenon, and in each instance the attack was relieved by adrenalin just as readily as when he had bronchiolar spasm throughout the lung.

When we are dealing with inspiratory retraction of the costal margin of one side, due to intrathoracic disease, a complete diagnosis is, of course, not directly implied, but we can be sure that the diaphragm has gained control of the costal margin. There is, however, an exception to this rule, and that is *synchia* between the diaphragm and the thoracic wall. If the pleural sinus is obliterated and the diaphragm has an attachment directly on the thoracic wall, then the insertions at the costal margin will no longer play a rôle in the control of the costal margin movement. Under these circumstances there will, of course, be no descent of the diaphragm, although the under surface of the arch of the diaphragm will be greatly accentuated in an upward direction, but the effective portion of the diaphragm will be that portion which lies between the central tendon and the *synchia* with the thoracic wall. Therefore the effective portion of the diaphragm may be horizontal when the concavity of the under surface is greatly increased. Under these circumstances the hypochondrium and costal margin will be drawn toward the median line during inspiration, although the leaf of the diaphragm on the affected side will occupy a much higher position than normally.

This movement of the costal margin can easily be shown experimentally on the dog by suturing the leaf of the diaphragm to a rib in the axillary and anterior axillary lines. This new fixation of the diaphragm will cause the costal margin to move toward the median line during inspiration. When the sutures are released the costal margin will again resume its outward movement. With this simple procedure the exact conditions of obsolete pleurisy with *synchia* between the diaphragm and the chest wall are reproduced.

DISPARITY OF MOVEMENT BETWEEN THE INNER AND OUTER PORTIONS OF THE COSTAL MARGINS. The curve of the diaphragm varies in its different portions. The muscular fibers of the diaphragm which take their origin from the central tendon, and which are inserted along the costal margin from the costal angle to the eighth costal cartilage, have a much less convexity than the fibers from the lateral and posterior portion of the diaphragm which are inserted on the costal margin from the eighth rib downward and outward. In studying movements of the costal margin it is essential not only to observe the direction of movement and symmetry of movement near the subcostal angle but also to observe the move-

ment of the costal margin below and external to the end of the eighth rib. Should the pericardial sac be enlarged or should there be globular enlargement of the heart the subcardial portion of the diaphragm will be depressed. The anterolateral portions of the diaphragm have much less curve than the lateroposterior portions, and for this reason it requires much less depression of that part of the diaphragm to give its respective fibers mastery of the costal margins where they are inserted. In pericarditis with effusion, when the fluid accumulates in sufficient quantities to be a factor in circulatory disturbances, the subcostal angle will be symmetrically narrowed during inspiration. The costal margins on both sides, from the angle to the eighth rib, will be drawn toward the median line, but below and external to the eighth rib the costal margins on both sides will move away from the median line.

We have had many opportunities to confirm this in patients with pericarditis with effusion and in cases of mitral stenosis and myocarditis. Tubercular pericarditis gives a particularly good opportunity to confirm this observation. These patients require repeated paracentesis of the pericardial sac. When there is a large accumulation the subcostal angle will narrow symmetrically during inspiration, and as fluid is withdrawn the angle will resume its normal widening; with reaccumulation of fluid a return to inspiratory narrowing is again observed. This phenomenon is of considerable service in estimating the significance of pericardial effusion. In pericarditis with effusion attended by inspiratory widening of the subcostal angle there is no indication for paracentesis for relief of pressure within the pericardial sac. There may be other reasons for paracentesis, such as establishing drainage, but we may be quite sure that relief of pressure is not demanded so long as there is inspiratory widening of the subcostal angle.

In children, whose diaphragms are flatter than in adults, a very moderate globular enlargement of the heart, as seen in mitral stenosis, is quite sufficient to cause inspiratory narrowing of the subcostal angle. It is not an uncommon experience to find in elderly persons, in combination with myocardial and vascular disease, a chronic bronchitis and emphysema. Under these circumstances one may be sometimes left very much in doubt in an interpretation of the significance of pulmonary disease and cardiac disease as sources of respiratory discomfort. Under these circumstances the percussion of the borders of the heart is attended with some difficulty, but if there is an inspiratory narrowing of the subcostal angle and the costal margins on both sides below and external to the eighth rib move in an outward direction we may be quite sure that the patient's air hunger is due more to cardiac disease than to pulmonary disease. If the pulmonary emphysema were sufficient to cause air hunger when the patient is at rest the costal margins in their entire extent would move toward the median line. This observation has been

confirmed in many instances by seeing the entire costal margin resume a movement in an outward direction after the employment of adequate doses of digitalis, although the physical signs of emphysema remained the same.

Thus far I have found only one exception to this rule, in a case of pericarditis with effusion, where there was synechia between the epicardium and pericardium over the anterolateral aspects of the heart, and there was a sacculated purulent pericarditis which was restricted to the posterior aspect of the heart alone. In this case the subcostal angle did not narrow during inspiration, although seemingly at autopsy there was a sufficient amount of fluid in the pericardial sac to cause it.

ASYMMETRY IN THE MOVEMENT OF THE SUBCOSTAL ANGLE WHEN THE LOWER AND OUTER PORTIONS OF THE MARGINS MOVE Laterally DURING INSPIRATION. The most common exhibition of asymmetrical movement of the subcostal angle is seen in enlargement of the left side of the heart when the right auricle is not enlarged and the right ventricle does not share equally with the left ventricle in its enlargement. Aortic valve stenosis and insufficiency may be attended by marked enlargement of the left ventricle while the right ventricle retains its normal size. Under these circumstances if the subcostal angle is observed it will be seen that the left border from the angle to the eighth rib will move less in an outward direction than the symmetrical portion on the right side, and the left side may be drawn toward the median line during inspiration as the symmetrical portion on the right side moves outward. Patients with left-sided lesions of the heart who have developed incompetency, with dilatation of the right ventricle and right auricle, will exhibit symmetrical narrowing of the subcostal angle during the period of incompetency, but after rest and digitalis it will be seen that the left margin will continue to move toward the median line but the right margin will move outward.

The only instances thus far that I have encountered in which the right ventricle and right auricle were greatly dilated without enlargement of the left heart were in soldiers at a casualty clearing station during the period of pulmonary edema from phosgene-poisoning. These patients developed acute dilatation of the right ventricle and right auricle without enlargement of the left heart, and consequently the costal margin of the right side from the angle to the eighth rib moved toward the median line during inspiration, whereas the left side retained the normal outward movement. After the administration of adequate doses of digitalin, that is, $\frac{1}{25}$ grain hypodermically, the right heart regained its normal size and the subcostal angle resumed its normal symmetrical inspiratory widening. This was, of course, in patients who had only moderate emphysema with pulmonary edema and did not have bronchiolar spasm.

Careful study of the relative movements of the upper and inner

portions of the two costal margins is a very great aid in estimating the relative size of the left and right sides of the heart, unless there should be an increase in the intra-abdominal pressure to prevent depression of the subcardial portion of the diaphragm.

During the past summer a patient was admitted to Lakeside Hospital suffering from acute septic endocarditis. There were no evidences of enlargement of either the left or right side of the heart, but the diagnosis of septic endocarditis without localization was made on account of the successful culture of pneumococci from the venous blood. In the absence of any evidences of localized infection elsewhere in the body the diagnosis of endocarditis was made by exclusion. At autopsy septic thrombi were found on the tricuspid valve and pulmonary valve and also thrombi on the wall of the pulmonary artery about one-fourth inch above the site of the valve. Although this was primarily an endocarditis involving the tricuspid and pulmonary valves the left ventricle and right ventricle retained their normal size.

Paralysis of the intercostal muscles will also cause asymmetry in the movement of the subcostal angle. A patient had severe syringomyelia, with kyphoscoliosis of the dorsal vertebrae, marked atrophy of the trapezii and all the scapulohumeral muscles, moderate atrophy of the muscles of the arms and pronounced atrophy of the muscles of the forearms and intrinsic muscles of both hands. The upper left thorax was stationary during inspiration. There was no inspiratory excursion from the first to the seventh rib inclusive, but from the eighth to the twelfth ribs inclusive there was a normal inspiratory excursion. From the subcostal angle to the eighth costal cartilage of the left side the border moved toward the median line during inspiration. From the eighth rib downward the costal margin moved outward during inspiration. This asymmetry of movement was interpreted as due to paresis of the upper intercostal muscles of the left side. It was quite conceivable in a patient who had an extensive syringomyelia of the cervicodorsal cord.

Another patient, a young woman, aged twenty years, at fourteen years of age had had an attack of poliomyelitis which left her with permanent paralysis and atrophy of the forearms, intrinsic muscles of both hands and scapulohumeral muscles of both sides; also the thigh and leg muscles were extensively involved. On the right side from the second to the seventh rib inclusive there was marked retraction of the ribs during inspiration. The eighth rib was stationary, but from the ninth to the twelfth rib there was an inspiratory movement in a normal direction. The costal margin of the right side, from the angle to the eighth rib, moved toward the median line with inspiration; and although the ninth rib was firmly attached to the costal border, from the ninth to the twelfth the costal margin moved away from the median line during inspiration. This asymmetry of movement in the inner portions of the costal borders was inter-

preted as due to paralysis of the upper seven intercostal muscles of the right side. This lesion was apparently acquired at the time of her acute poliomyelitis.

The following case exhibited very unusual respiratory excursion of the costal margin. The patient had an old syphilitic disease of the myocardium and aorta, and in addition to this had acquired a tuberculous pleurisy of the left side. On entering the hospital it was found that during inspiration the right costal margin, from the angle to the eighth rib, moved toward the median line, and the left costal margin, from the angle to the eighth rib, moved very slightly away from the median line. The lower and outer part of the right margin moved away from the median line and the lower and outer portion of the left side moved toward the median line. After 1800 c.c. of bloody and turbid serum were removed from the left thorax, the entire right costal margin moved away from the median line during inspiration and so did the entire left costal margin, but it was observed that the upper and inner part of the left costal margin moved less in an outward direction than the margin of the right side. After the fluid had been removed a roentgen-ray picture revealed enlargement of the ascending and transverse arch of the aorta. The heart occupied a transverse position, but the base of the heart did not come to the right of the sternum. The diaphragm of the left side revealed a silhouette much higher than that on the right side and there was marked thickening of the pleura over the entire left side. Our interpretation of the excursion of the costal margins when he entered the hospital was that the retraction of the upper and inner portions of the right costal margin was due to depression of the right anterolateral portion of the diaphragm on account of the great cardiac displacement to the right. Prior to the thoracic paracentesis the right border of the heart came nearly to the right nipple line, and after paracentesis, when the heart came back to the normal position, the entire right border resumed its normal inspiratory excursion. On the left side the lower and outer portion of the costal margin resumed a normal outward movement during inspiration after the fluid had been withdrawn from the chest, but the upper and inner portion of the left costal margin retained about the same inspiratory movement before and after paracentesis on account of synechia between the anterolateral portion of the diaphragm and the thoracic wall, and this synechia did not permit the anterolateral portion of the diaphragm to be depressed when the pleural effusion was present, nor did it rise after the fluid was aspirated. This rather bizarre movement of the costal margin is described because it illustrates how accurately the curve of the diaphragm in its different portions is reflected by the inspiratory movement of the costal margins where the affected parts of the diaphragm are inserted.

SUMMARY. A summary of the whole matter is that in interpreting the inspiratory movements of the costal margins one must study the

symmetry and asymmetry not only of the entire costal margins but of the inner and outer portions of each costal margin. Movements of the costal margins are modified with changes in the curve of the plane of the diaphragm, by paresis of either the diaphragm or the intercostal muscles and by synechia between the diaphragm and the thoracic wall. Such studies improve the accuracy with which one differentiates between infraphrenic and supraphrenic disease, and enable one also to estimate the conformation of the heart and the size of the pericardial sac and to differentiate between lesions which cause phrenic displacement and those which do not modify the plane of the diaphragm.

EARLY LESIONS IN THE GALL-BLADDER.¹

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AND

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THE study of early pathological conditions in the gall-bladder has been greatly facilitated by cholecystectomy, an operation which many surgeons have deemed advisable in preference to cholecystostomy. In their experience many patients in whom the organ had been drained returned to them with symptoms unrelieved. The desired relief in such cases seems to have been accomplished, at least in a much higher percentage, by the secondary complete removal of the organ. This experience with such cases following a secondary cholecystectomy has led, in the last five years, to the custom of primary cholecystectomy in preference to cholecystostomy in patients with a visible lesion and also in some patients in whom there is no visible gross pathology but a definite clinical picture pointing to this organ, plus enlargement of lymphatic glands along the ducts.

From January 1, 1913, to January 1, 1919, 4998 gall-bladders were removed at the Mayo Clinic. Of these, 4824 (96.5 per cent.) showed unquestioned gross pathological lesions (Table I).

In this series of conditions it may be seen there were 157 with slight lesions and 17 grossly "normal," most of which showed definite changes in the villi on examination with a high-power dissecting microscope or in microscopic sections.

¹ Presented before the American Gastro-enterological Association, Atlantic City, June, 1919.

CLASSIFICATION OF 4998 GALL-BLADDERS.

	Specimens.
1. Cholecystitis catarrhalis acuta	17
Cholecystitis catarrhalis acuta, with "strawberry" appearance	9
2. Cholecystitis catarrhalis subacuta	112
3. Cholecystitis catarrhalis chronica	2021
Cholecystitis catarrhalis chronica, with "strawberry" appearance	948
Cholecystitis catarrhalis chronica, with adenoma in the wall	1
Cholecystitis catarrhalis chronica, with accessory fundus	1
Cholecystitis catarrhalis chronica, with diverticula	4
Cholecystitis catarrhalis chronica, with old perforation	1
Cholecystitis catarrhalis chronica, with very slight lesion	38
Cholecystitis catarrhalis chronica (?)	157 (3.10%)
4. Cholecystitis catarrhalis papillomatosa	212
Cholecystitis catarrhalis papillomatosa, with "strawberry" appearance	129
Cholecystitis catarrhalis papillomatosa, with "strawberry" and cystic appearance	1
Cholecystitis catarrhalis papillomatosa, with a diverticulum	1
Cholecystitis catarrhalis papillomatosa, subacuta	1
Cholecystitis catarrhalis papillomatosa, malignum	1
Cholecystitis catarrhalis papillomatosa, malignum (?)	1
5. Cholecystitis catarrhalis carcinomatosa	22
Cholecystitis catarrhalis carcinomatosa (?)	1
6. Cholecystitis chronica	900
Cholecystitis chronica, with honeycomb appearance	8
Cholecystitis chronica, with perforation of wall	1
Cholecystitis chronica, with calcification of wall	1
7. Cholecystitis chronica cystica	112
Cholecystitis chronica cystica (empyema)	24
8. Cholecystitis acuta	81
Cholecystitis acuta, with perforation of wall	1
9. Cholecystitis purulenta necrotica	168
Cholecystitis purulenta necrotica, with "strawberry" appearance	5
10. Cholecystitis ulcerosa	1
11. Cholecystitis epitheliomatosa (with gall-stones)	1
12. "Normal" gall-bladders (gross diagnosis)	17 (0.31%)

The early changes in the gall-bladder consist of:

1. Congestion and edema of the villi frequently associated with a bulbous appearance (Figs. 1, 2, 3 and 4) which, on casual gross examination, makes the villi appear cystic. Occasionally they are cystic. The mucosa in advanced stages of this congestion and edema sometimes presents the appearance of being covered with small fish-scales (Fig. 5), an appearance which is due to the presence of a lipoid infiltration in the stroma or epithelial cells (Figs. 6, 7 and 8).

2. Local or general slight degree of lymphocytic infiltration which manifests itself only in a slight enlargement of the villi (Figs. 9 and 10) and a cloudy or duller appearance.

3. Local or general slight degree of lymphocytic infiltration is seen in the mucosa alone, which might possibly be considered normal, since the mucosa probably contains a certain number of lymphocytes; but when seen in association with a lymphocytic infiltration in the submucosa, muscularis and subserosa (Fig. 11) very probably indicates a pathological condition. Such infiltra-

tion is associated with a bulbous appearance of the villi or a thickening of the bases of the villi (Figs. 12 and 13).

4. The presence of fibrosis (Fig. 13) in the villi which usually are not thin and tentacular (in sections) like those of the perfectly normal organ. The fibrosis sometimes extends into the submucosa, muscularis and subserosa (Fig. 11).

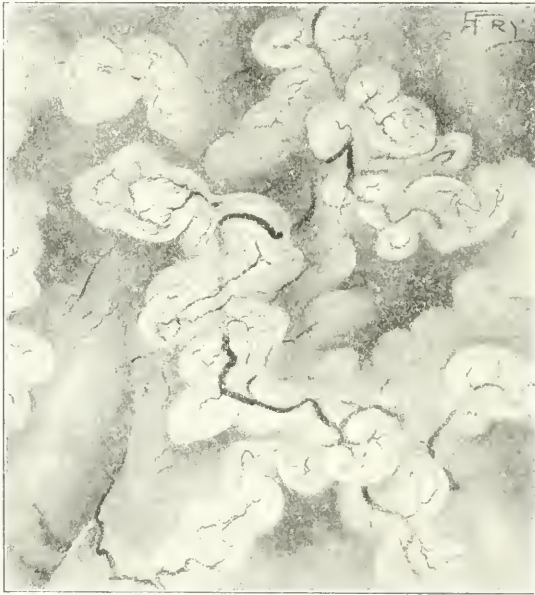


FIG. 1.—Villi of a gall-bladder in an early stage of congestion and edema.

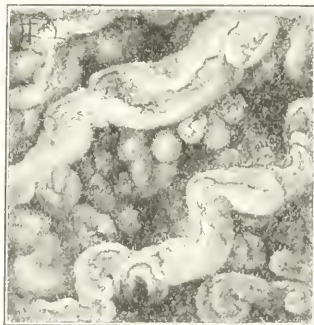


FIG. 2.—Villi of a gall-bladder, showing congestion and distortion in early cholecystitis.

5. The presence of lymphocytic infiltration and fibrosis, such as described above, plus the presence of a finely granular or lipid substance in the epithelium (Figs. 6 and 7) or just below the epithelium in the mucosa (Fig. 8).

6. The presence of slight or no lymphocytic infiltration and fibrosis plus the presence of large spheroidal cells filled with finely granular lipoid substance in the mucosa and sometimes in the

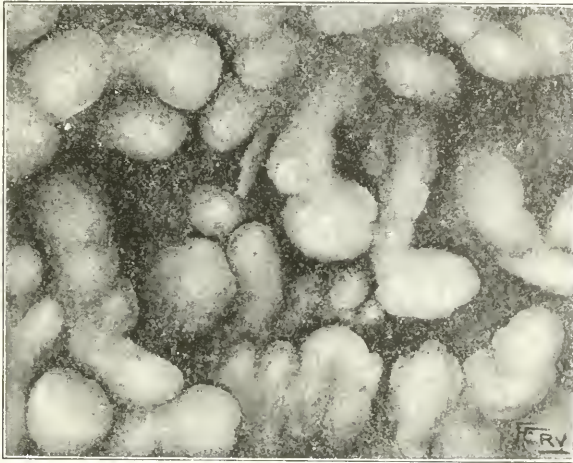


FIG. 3.—Edematous villi having a bulbous appearance and showing pale areas which are due to deposits of a lipoid substance in the epithelium or just beneath the epithelium in the connective-tissue stroma.

submucosa (Fig. 8). These cells are similar to those which have been described in the so-called "strawberry" gall-bladder,^{2,3} and in papillomas.¹ This substance may not be visible grossly, but



FIG. 4.—Villi in an edematous condition.

may sometimes be detected with the high-power dissecting microscope (Fig. 3). It is the substance which gives villi in the "strawberry" gall-bladder and papillomas their yellow or white appearance.

The conditions which have been described above do not alter the gross exterior of the organ, nor do they alter greatly the internal appearance to the naked eye.

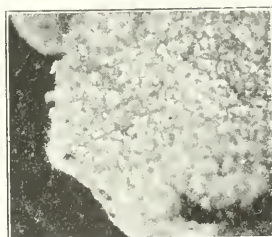


FIG. 5.—A condition of edema of the villi associated with deposits of lipid materia in the epithelium and stroma.

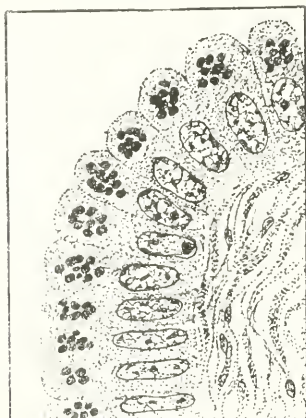


FIG. 6.—Diagrammatic sketch, showing the location of lipid substance in the epithelium. Made from a section stained with scarlet R.

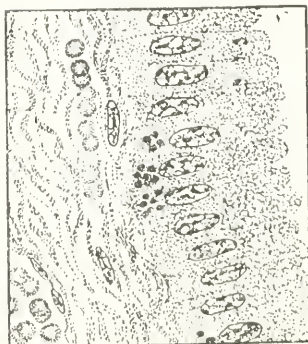


FIG. 7.—Diagrammatic sketch, showing the location of the lipid substance in the cells but near the stroma.

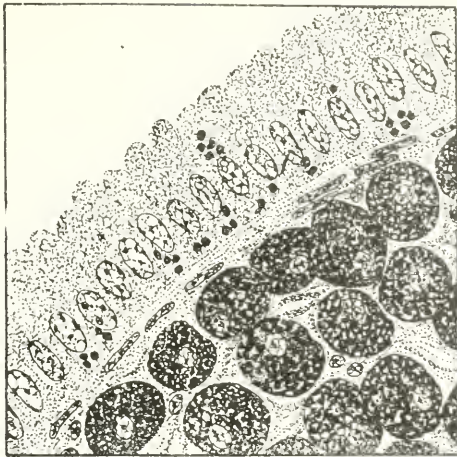


FIG. 8.—Diagrammatic sketch, showing the lipid substance in the epithelium and also in the cells of the stroma.



FIG. 9.—Section through the mucosa of a gall-bladder in a mild condition of chronic catarrhal cholecystitis. The villi contain many lymphocytes.

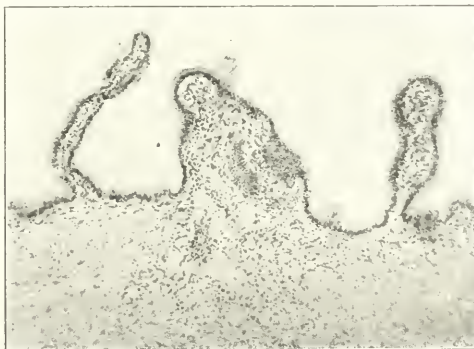


FIG. 10.—Section through the mucosa of a gall-bladder, showing lymphocytic infiltration of the villi and the underlying stroma.

It is this group of slight pathological reactions which has made many surgeons, who believe that a cholecystectomy is the opera-

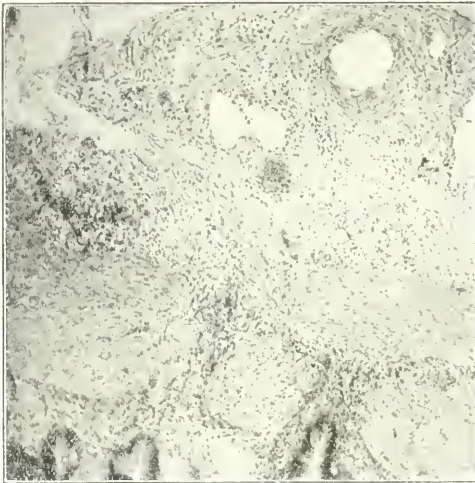


FIG. 11.—Section of the submucosa of a gall-bladder, showing lymphocytic infiltration and fibrosis.

tion of choice in cholecystitis, somewhat slow in carrying out their belief in practice. Also, it is probably this group which is so fre-



FIG. 12.—Section through the mucosa of a gall-bladder, showing lymphocytic infiltration and fibrosis in the villi. There is a glandular increase and the villi have lost their tentacular appearance.

quently seen in association with stones and has led many observers to believe that stones occur in perfectly normal gall-bladders.

With our present knowledge we are not prepared to say definitely that such early conditions alone present sufficient symptoms to make a definite clinical syndrome, especially in view of the fact that recent studies made by one of us (MacCarty) indicate that such conditions in the gall-bladder are also associated with somewhat similar changes in the extrahepatic and intrahepatic bile ducts, which might readily interfere with hepatic function and therefore produce clinical disturbances. As a matter of fact such patients do present some general disturbances which clinicians refer to under the broad heading of toxemia.

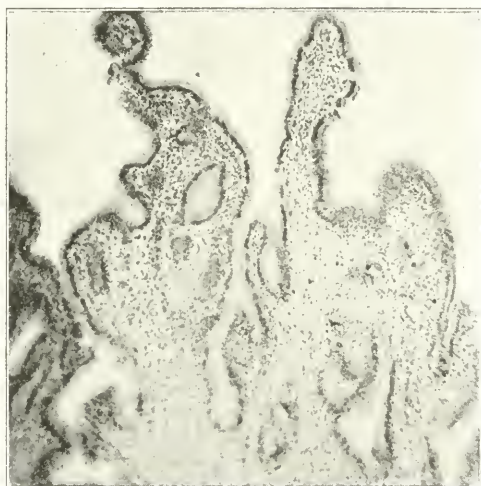


FIG. 13.—Section through the mucosa of a gall-bladder, showing lymphocytic infiltration, fibrosis and distortion of the villi.

This paper has for its object the stimulation of greater interest and more detailed research in conditions of the bile passages which have heretofore been mistaken for normal.

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THE RESULTS OF OPERATIONS FOR CHRONIC APPENDICITIS: A STUDY OF 555 CASES.¹

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THIS study is based on two questions: (1) How often does the removal of a supposedly diseased appendix fail to relieve symptoms or improve the patient's condition and (2) what are the reasons of such failures and how can we avoid them?

Removal of the appendix is very common today. The great bulk of these operations is very easy and can be readily done even by those with little technical skill and a minimum knowledge of surgical principles and morbid anatomy. The immediate convalescence is easy and the psychic results are also a factor. The operation is particularly gratifying as a prophylactic measure when well-defined attacks have given anxiety lest the subject should be "caught" in the more serious or even tragic phases of an acute attack.

In a second class the removal of the appendix brings relief to symptoms which are indirect, particularly of the digestive apparatus. According to Moynihan's dictum, most of the ulcers of the stomach are situated in the right iliac fossa.

Both of the above classes furnish a legitimate and gratifying field, and if operations were limited to them there would be but few failures to record. Operations for chronic appendicitis have also given good results in that the operation, if conducted as an exploratory operation (as it should generally be), has resulted in removing an appendix, normal or altered, and in remedying at the same time some other important morbid process.

Unfortunately the second class is not sharply defined, and there is also a third and rather vague class—which might be called the symptomless class—in which the removal of the appendix has apparently greatly benefited the patient's general condition.

Owing to the vagueness of this third class, numerous patients are subjected to removal of the appendix needlessly and recklessly. Consequently a certain proportion of bad results must follow to the natural dissatisfaction of the patient, often to his great detriment, if a condition really needing surgical interference (*e. g.*, ureteral stone) was overlooked, and to the discredit of the profession. Witness the laws of a Western State which inflicts penalties for needless appendix operations.

An incorrigible humorist, the late Dr. Alexander Johnson, once answered a layman's inquiry as to the functions of the appendix

¹ Read before the New York Academy of Medicine, January 15, 1920.

by saying: "It contributes largely to the support of a noble profession." Many a truth is spoken in jest, but I dislike to think of our profession being either the principal or accessory to such a joke, and in this paper I hope to demonstrate what we have done in our hospital service toward lessening the opportunities for such jibes.

The thoughtful and conscientious element of the profession has for some time recognized that appendix operations not infrequently give bad results; but there has not been enough frank confession of these results or systematic attempts to obtain a remedy. It is natural and legitimate to err on the side of safety, and it is a fearful thing to tell a patient he has no reason to worry over his appendix and have the patient subsequently go through a severe acute operation or possibly die. Perhaps it will be better to resign ourselves to doing a certain number of these needless operations for the sake of safety. I believe we can reduce them by more painstaking methods of study of such conditions, particularly of the more common sources of error.

One great help is the study of results. Soon after the establishment of my follow-up system² in my service at the New York Hospital, in 1914, it became painfully evident that we were getting too many unfavorable reports in our chronic appendicitis cases, and measures were instituted along the lines to be described later for this improvement. The preparation of a formal study of a large number of conditions was delayed by war conditions, and it was not until this paper was undertaken that the full significance of many of the features necessary for improvement was realized.

Table I shows that of late our results have been much better. Also the greater degree of exploration we are now making by abandoning the small or interval incisions. We are also doing either fewer operations for chronic appendicitis or operating on cases under a different and correct diagnosis.

TABLE I.

Year.	No. of cases.	Per cent. unsatisfactory.	Per cent. of McBurney incisions.
1913	70	28	74
1914 ³	63	23	65
1915	98	28	21
1916	100	26	36
1917	119	24	35
1918	84	20	14
1919 (6 months)	21	11	10

This paper is based on a study of 555 patients in the ward (no private) service of the First Surgical Division of the New York

² *Annals of Surgery*, September, 1916, No. 3, vol. lxiv; December, 1919, No. 6, vol. lxx.

³ After my follow-up system had been in effect a year the McBurney incisions dropped notably.

Hospital, January 1, 1913, to July 1, 1919. Of this number we have no record of 126 patients.⁴ We have good reasons, to be stated later, for believing that our best results were obtained in the patients who failed to report, consequently the basing of end-results on only the 426, restricting the reported number, makes the results seem worse than they really are.

We have preferred to take the facts as they appear in our records rather than yield to the temptation of juggling of figures in any way. Several of our cases are obviously not cases of chronic appendicitis, the main operation being something else, but the discharge cards read (as a result of carelessness) "Chronic appendicitis," and are so recorded. (The service was kept going with great difficulty during the war.) The work has been done by myself, the two associate surgeons, Drs. J. M. Hitzrot and B. J. Lee; Dr. C. E. Farr, assistant surgeon, and, for a short period, by Dr. L. A. Wing.

For the sake of clearness the cases have been divided into five categories:

Class A (259). *Excellent*. Patients who on reëxamination present no complaints whatsoever.

Class B (65). *Satisfactory*. No complaints pointing to their former condition, but have some minor complaint.

Class C (102). *Unsatisfactory*. Patients who have not been improved.

Class D (126). *Unknown*.

Class E (3). *Deaths*.

All classes have been studied under the same headings. Table II gives a summary of the principal findings common to all classes.

We note that the age distribution seems to be about the same in all classes, the largest percentage of operations being performed on patients between the ages of twenty and thirty. It will be noted also that the unsatisfactory cases were the ones averaging the longest stay in the hospital. This fact probably means that their cases were obscure and reluctance was felt to operate on them without sufficient observation.

Under "Special Examinations" we mean more particularly gastric analyses and bismuth series of the gastro-intestinal tract. There is not much difference in any of these classes, the lowest being the unknown, occurring largely in our first year before we had systematized our hospital service.

By "Further Exploration" is meant that a record exists in the history of the operation that investigations of the abdomen were made besides the removal of the appendix. Considerably less of this exploration apparently was made in the classes "Satisfactory" and "Unknown," probably owing to the very obvious pathological

⁴ Many of these are 1913 patients who could not be traced after a period longer than the usual three months.

condition of the appendix as noted in the percentage of those conditions found.

TABLE II.

	Excellent, per cent.	Satisfactory, per cent.	Unsatisfactory, per cent.	Unknown, per cent.
Male ⁵	70	14	16	
Female	56	16	28	
Nationality (English speaking)	43	49	29	38
Age:				
1 to 10 years	1	2	2	2
10 to 20 "	29	23	27	22
20 to 30 "	46	56	48	52
30 to 40 "	17	12	15	20
40 to 50 "	5	3	4	2
50 to 60 "	2	2	1	2
60 to 70 "	2	3	
History of well-defined attacks	51	51	35	47
Analysis of chief symptoms:				
Pain, R. L. Q.	50	35	30	50
Pain and vomiting	15	15	13	16
Pain in epigastrium	7	5	9	6
Pain and constipation	9	25	8	5
Average number of days spent in hospital before operation	2.57	2.53	3.19	2.30
Special examinations	46 ⁶	54	56	36
Kind of incision:				
McBurney	37	22	31	52
Large	63	78	69	48
Appendix pathological	85	75	63	77
Further exploration	52	83	73	52
Complications	22	38	22	18
Subsequent admission	2	0	25	2
Subsequent operation	1.5	..	5	2

By "Complications" we mean the existence or remedying of other conditions whether intra-abdominal or not.

⁵ The percentage of satisfactory cases was 72 per cent. for women, 88 per cent. for men.

⁶ Diagnosis more obvious in lesser number of tests. Notes have all been more precise in the more recent years since we have learned the necessity of precision of data.

POINTS OF SPECIAL INTEREST IN EACH CLASS.

Class A. Excellent, 259.

The larger proportion of males. Men have fewer conditions to obscure the diagnosis. There are more men carrying a really diseased appendix. Of our 820 operations for *acute* appendicitis 64 per cent. were men.

Larger proportion, as in Class B, of English-speaking people (who are in a minority in the New York Hospital). As the greatest single factor in diagnosis is a clear and reliable history we are much handicapped by the limitations of speech and intelligence of our patients. The larger proportion of histories giving definite pain, 50 per cent., in the right lower quadrant.

Definite record of the removal of an obviously pathological appendix, 85 per cent., compared to the 63 per cent. in the unsatisfactory Class C. These findings are dictated in the operating room in the hearing of the assistants and onlookers.

Only 2 per cent. of these patients were readmitted (for other conditions), while 25 per cent. of unsatisfactory, Class C, came back.

Class B. Satisfactory, 65.

Class B shows substantially the same features, but is less marked as regards the three main features, per centage of males, pathological appendix and pain in R. L. Q. It is in this class of cases that we may have occasionally overlooked some cause for their minor complaints.

ANALYSIS OF POSTOPERATIVE COMPLAINTS.

Complaint.	No. of cases.
Constipation	29
Gynecological conditions	6
Pain elsewhere	3
Backache	4
Bladder trouble	2
Pain in scar	4
Indigestion	6
Vague complaints	11

Of the group classed as satisfactory, but exhibiting minor complaints, we note the largest (with the exception of constipation), 11 cases, as absolutely vague, such as "having a burning sensation when she wears corsets." Six are gynecological troubles, such as leucorrhœa and lacerated cervix. A little pain in scar or slight indigestion make up the next largest groups.

Class C. Unsatisfactory, 102.

This is the class which is really the subject of the paper and deserves the fullest analysis. All reasonable efforts were made to have the patients subject themselves to more examinations, particularly those bearing on symptoms complained of, *e. g.*, gastric analyses and roentgen ray for gastro-intestinal conditions, also

roentgen ray of the urinary tract. Twenty-five per cent. were persuaded to reënter the hospital for observation. The results are shown in Table III.

TABLE III.—SUBSEQUENT ADMISSIONS AND OPERATIONS, 26.

Gastroptosis, 3 cases. All cases had gastric analysis and bismuth series.

Neurasthenia and rheumatism, 1 case.

Postoperative constipation, 1 case. Gastric analysis.

Readmitted for bismuth series, negative result, 4 cases.

Adhesions of peritoneum, no operation, 5 cases.

Five cases had bismuth series. Negative, with exception of one case, which showed possibly slight gastroptosis.

Adhesions of peritoneum, operation, 3 cases.

1. Operation showed adhesion of omentum to scar. Adhesion divided. Six months after second operation patient still complained of indefinite pain on the right and the left side of the abdomen.

2. Operation showed adhesions of the peritoneum and abscess of the colon. Nine months after this operation the patient was again admitted, with diagnosis of adhesions. Operation thought inadvisable.

3. Two operations for adhesions. First fourteen months after appendectomy, second a year and seven months later. Readmitted a third time, with same diagnosis, but operation was thought inadvisable.

Removal of cystoma of right ovary, 1 case. "Neurasthenic wreck."

Cholecystectomy for cholelithiasis, 1 case. Six months after this second operation the patient came back, complaining of symptoms which point to adhesions.

Roentgen ray of sacro-iliac joint suspicious of arthritis, 1 case.

Roentgen ray of kidney negative, 3 cases.

Possible ulcer of stomach, 2 cases.

Bismuth series and gastric analysis.

Readmitted for investigation, diagnosis unknown, 1 case. Gastric analysis.

This series of readmission cases (the severer) showed therefore:

Four cases of gastroptosis (3 cases had pathological appendix).

Four presumptive postoperative adhesions.

One cholelithiasis.

One cystoma of ovary.

Three definite trouble from adhesions as proved by operation

We may say, therefore, that mistakes were made in not looking for or missing the cholelithiasis and the ovarian cyst, and that it was probably a mistake to have operated at all on the cases of gastroptosis.

It is impossible to judge whether adhesions are due to original conditions or to the appendectomy. Turning in of the stump of the appendix, as is our custom, leaves a minimum of irritation, but I have seen severe adhesions following.

In patient's not reëntering the hospital further study and examinations were unsatisfactory. Many flatly refused any form of examination, particularly those subjecting them to discomfort and loss of time. Expense was also a drawback, as these patients are required to pay for their roentgenray examination. As a consequence we are quite often unable to get an intelligent impression of the results, particularly in distinguishing ordinary kicks and neurotic manifestations.

Table IV shows the grouping of complaints, with data as to sex and condition of appendix:

TABLE IV.

Unsatisfactory (chief complaint after operation).	Male.	Condition of appendix.		Female.	Condition of appendix.	
		Path.	Not path.		Path.	Not path.
Pain in region of gall-bladder	1	..	1	2	2	
Pain over right kidney	2	1	1
Diarrhea	1	..	1
Pain in epigastrium	4	3	1	3	2	1
Great many vague pains and symptoms	5	4	1	16	8	8
Diastasis of recti	1	..	1
Severe pain just below umbilicus. Wound still discharging	1	1
Severe pain in right side, especially during menstrual period	3	3	..
Pain in appendix region	1	1	..	19	14	5
Pain in right lumbar region and discomfort about scar	1	1	..
Abdominal pain and cramps	1	..	1	6	3	3
Pain both sides of abdomen	1	1	..
Pain in region of splenic flexure	1	..	1
Feels sick, loss of weight, appetite poor and bowels bad	1	..	1
Pain on left side, headache, poor appetite	1	1	..
Nausea and loss of weight	1	..	1
Constipation, poor appetite, pain in scar	1	1	..
Indigestion, obstinate constipation, pain in back	1	1	..
Constipation, headache, vomiting	1	..	1
Great deal of tenderness in scar	1	1	..
Cramps at night, loss of sleep, loss of weight	1	1	..
Gas and soreness, R. L. Q.	1	1
Great deal of pain in right groin	1	1	..
Same pain as before operation	8	5	4	12	9	3
Pain and discomfort in lower right abdomen	2	1	1

Analysis of chief complaint after operation shows pain in some form as the main factor. It comes mainly under four headings:

1. Great many vague pains and symptoms, seen mostly in women (16), 21 cases.
2. Pain in appendix region (19 women, 1 man), 20 cases.
3. Same pain as before operation (8 men, 12 women), 20 cases.
 - (a) Pain in epigastrium, 1 case.
 - (b) Abdominal pain, 2 cases.
 - (c) Pain in right inguinal region, 1 case.
 - (d) Discomfort in lower abdomen, 1 case.
 - (e) Pain in right iliac region, 1 case.
 - (f) Indigestion and gas, 1 case.
 - (g) Pain in R. L. Q., 13 cases.
4. Pain in epigastrium (4 men, 3 women) 7 cases.

Of the 65 cases in which the appendix was obviously pathological, 66 per cent. had further exploration at the time of the operation.

Of the 37 cases in which the appendix was not obviously pathological, 84 per cent. had further exploration at the time of the operation.

In group 1 and 2 it is legitimate to believe that most of these were unjustified complaints, for the sake of making a "kick" or "nerves."

In groups 3 and 4 it is more likely that the real cause was overlooked. These two classes showed a clean-cut preponderance of definitely pathological appendices, hence the operator probably did not make so thorough a search for a coexistent lesion as he would have felt it necessary to make if he had found originally an innocent-looking appendix.

In this class exploration of the abdomen showed a number of conditions which were remedied, some non-remediable by operation, and in a smaller group it is not obvious if any attempt was made to remedy the trouble. In 40 cases exploration was negative. Most of the troubles were gynecological or due to adhesions. On the whole one gets the impression that the explorations were thorough and the conditions found generally satisfactorily remedied, so that the poor results in this group were not due to careless or insufficient operation.

How shall we explain the results in this group in which in the majority (63 per cent.) the appendix is stated to be definitely pathological? I think it is fair to say that in a certain number there were in addition to a true appendix other conditions which we overlooked, lulled into a false security by the fact that there was a definitely pathological appendix and therefore did not make the operation a true exploratory laparotomy with a large incision allowing of a more nearly complete examination, particularly of the upper abdomen. The frequent coexistence of disease of the upper abdomen with a chronic appendicitis is today well established. Every surgeon of large experience can relate coexistence of a certain number of cases

of acute appendicitis, with other conditions which give rise to the "acute abdomen." Offhand I can remember two acute appendices coexistent with ruptured ectopic, also coincident with a torsion of an ovarian cyst, also a recent acute appendix, with a subacute perforation of the duodenum. The lesson, therefore, is to do more thorough work, even if a definitely chronic appendix is found, look for other possible lesions, particularly in women and those past the second decade, and more particularly the third. At an earlier period gastro-intestinal conditions, biliary lesions, diseases of the pelvic viscera, especially the sequelæ of pregnancy, are rare.

We do not have to be too apologetic for the results of Class C (unsatisfactory cases); that 63 per cent. of them were safely and on the whole comfortably rid of a definitely bad appendix is by no means a surgical failure.

Class D. Unknown, 126.

This class would probably represent the most satisfactory cases, as it corresponds largely to the conditions noted in "Class A," or Excellent, the large proportion of males, history of well-defined attacks, pain in the right lower quadrant and obviously pathological appendix. A large proportion of these patients were operated on in 1913, but were not sent for until a much later date, and therefore could not be traced.

Class E. Deaths, 3. The three deaths were due to:

1. Postoperative intestinal obstruction.
2. Acute general peritonitis and lobar pneumonia.
3. Cellulitis of abdominal wall, multiple intra-abdominal abscesses and pulmonary tuberculosis. The sepsis was the result of using unsterilized material at operation, due to the mistake of a green orderly.

A fourth death might be included technically in this series under chronic appendicitis. It is, however, such a faulty diagnosis that I feel justified in eliminating it. The patient entered the hospital and was operated on under the diagnosis of chronic appendicitis. Operation, March 7, 1916, the appendix could not be found. Re-entered the hospital June 8, 1916, for an operation for repair of a fecal fistula, the lesion at that time being diagnosed as tuberculosis of the intestines. November 2, 1917, he underwent another operation for the cure of the fecal fistula and ventral hernia, from which he died.

To avoid disappointing results after operations for chronic appendicitis I recommend:

1. A comprehensive and detailed history.
2. A complete and thorough physical examination, including all refinements of diagnosis.
3. Exercise caution in undertaking operation on women as compared to men.

4. Exercise caution, particularly in the more mature patients, particularly women. In this class other lesions may coexist or may be mistaken for appendicitis.

5. Avoid the neurasthenies of any age or sex.

6. Exercise particular restraint when there is no clear and reliable history of well-defined attacks, particularly of localized pain accompanied by nausea or vomiting.

7. Make a good-sized incision, and, even if a frankly pathological appendix is found, look for other possible lesions.

8. If no obviously pathological appendix is found, do not cease looking for other lesions until every other possibility has been exhausted; make a supplementary incision if necessary.

NOTE. In discussing this paper, Dr. C. H. Peck alluded to the possibilities of trouble due to adhesions possibly provoked by the irritating effects of tincture of iodine carried from the surgeon's gloves from the skin.

It suddenly occurred to me that the explanation of the very marked improvement in results for the six months ending July 1, 1919 (11 per cent. of unsatisfactory results as compared to 20 per cent. in the year 1918), might very well be due to the absence of this irritating property of iodine, as in December, 1918, we instituted in our service the use of 5 per cent. alcoholic solution of picric acid for the skin. We are very sure of the superiority of this method as regards irritation of the skin. Of nearly 1500 cases we have had only one that showed any irritation at all, and that extremely trivial. Experiments are now being conducted by Dr. Charles E. Farr, assistant surgeon, concerning the comparative irritation of picric acid on the peritoneum.

Should the presumption raised by this improvement in our figures be confirmed by further experiments, especially by others, a very notable improvement in operative technic would ensue. As noted before, the chief and very constant complaint of patients returning for observation who were not satisfied by their operation is pain, and it might well be pain due to the irritation of the iodine, as it is particularly noticeable that the pain so frequently mentioned is at the operative site, although an unquestionably pathological appendix has been removed.

It is also interesting to contrast the practical absence of complaints of our patients who have been operated on for acute appendicitis. When reexamined they are quite free from complaints. Of course, with an acute operation little or no exploration is usually made and only a very small field is exposed.

NOTES ON GASTRIC SECRETIONS IN NEUROCIRCULATORY
ASTHENIA.

BY JOHN H. MUSSER, JR., M.D.,

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THE problem of neurocirculatory asthenia has probably aroused more discussion than any other in the realm of internal medicine during the last year of the war. The English, under the leadership of Mackenzie and Lewis, early attacked the problem and studied it from many angles. In the United States active interest became acute with the examination of large numbers of soldiers for admission to the service and with the return of soldiers from France who had been unable to stand the strain on account of the appearance of certain symptoms referable in part to the cardiovascular system and in part to the nervous system. The question of the pathogenesis of the condition has aroused particularly earnest study, but nothing definite has been determined; indeed, the viewpoint of English and American students of the problem seems to be extremely divergent. The one point upon which there is a certain unanimity of opinion is that the individual suffering with neurocirculatory asthenia is, to start with, constitutionally a neurotic or substandard type. In the United States many recruits were weeded out by examining boards because they were of this type and suffered from many symptoms in addition to those referred to the heart. Many soldiers were sent to France who were of this type, but in whom the manifestations of the disorder remained latent until they were put in position of acute stress. Under such conditions they broke down and were sent to the rear.

The uniformity with which soldiers developed symptoms of neurocirculatory asthenia after engaging in actual combat has led many of the internal medical men, including Lieut.-Col. A. E. Cohn, the cardiac consultant of the A. E. F., to look upon the condition as a fear neurosis, pure and simple. A soldier, constitutionally inferior to start with, under the stimulus of fear, becomes extremely neurotic. Various symptoms develop, all without anatomical basis, and many referred to vagus irritability, and, as Friendländer and Freyhof¹ say, without any one symptom predominating. In a short time the soldier becomes introspective, self-centered and the condition of neurocirculatory asthenia becomes full-blown.

As the relationship between the nervous system and the stomach is so close it was thought that, considering these cases as types of marked disturbance of the nervous system, with particular emphasis on the vagus, the study of the gastric secretions, if the gastric secre-

¹ Intensive Study of Fifty Cases of Neurocirculatory Asthenia, *Arch. Int. Med.*, 1918, xxii, 693.

tion was found disturbed, could throw some light on the question (1) of vagal irritability and (2) would possibly add further clinical evidence, which would aid in determining the diagnosis of a condition which at best represents a group of symptoms without being a definite clinical entity.

To review briefly and succinctly the physiology of the stomach, it will be recalled that Pawlow² first demonstrated that gastric secretion is under the control of the nervous system and that the secretory fibers are in the vagus. Howell³ says that secretion is due to the action of the vagus, as can be shown readily by animal experiment. Further steps in the physiology of secretion include the secretion from secretagogues contained in the food and from those in the products of digestion. After the usual test-breakfast the gastric acidity usually reaches a total of about 60 in terms of decinormal sodium hydrate solution and about 45 for the free hydrochloric. Hyperacidity, that is, high acid contents of the gastric contents, is frequently met with in conditions unaccompanied by structural changes in the stomach or other abdominal viscera. It is, according to Hewlett,⁴ "particularly frequent in young individuals and in those of a nervous temperament . . . whenever they are placed under an unusual nervous strain and those who follow occupations that involve much care and worry. . . ." A young soldier of a constitutional nervous temperament subject to emotional disturbance, returned from the active front, represents perfectly the picture described by Hewlett of those likely to suffer from symptoms of hyperacidity, and it is just such a soldier who is likely to be the subject of neurocirculatory asthenia.

Fractional gastric analyses were made upon many soldiers suffering from simple tachycardia, tachycardia from poisoning by inhalation of deleterious gases and similar conditions. Eleven soldiers presented the characteristic subjective symptoms and objective findings of undoubted neurocirculatory asthenia. Some of these latter individuals were seen in consultation with Lieut.-Col. Cohn. As controls the gastric secretions of eleven soldiers suffering from minor surgical and medical conditions were studied. The clinical records of two patients may be selected as examples of the general type of case of neurocirculatory asthenia with which we were dealing.

ABSTRACT OF FIELD MEDICAL CARD.

CASE I.—H. B., Corporal, Company M, 166th infantry.

Camp Hospital No. 30. Date of admission, August 27, 1918.

Diagnosis: F. U. O. Chronic endocarditis.

Base Hospital No. 116. Neurocirculatory asthenia; effort syn-

² The Work of the Digestive Glands, 1902, London.

³ Text-book of Physiology, 1918, 6th edition, Philadelphia, p. 775.

⁴ Functional Pathology of Internal Diseases, New York, 1918 p. 143.

drome. Date of admission, September 11, 1918. Has had pains in chest and becomes easily exhausted for the past three months. Gets up at night fighting for air.

Examination. Apparently dyspneic; hands cold and purplish. Cardiac action fast but regular as to rhythm. No murmurs. Lungs negative. Abdomen negative.

September 14, 1918, evacuated.

Base hospital No. 20. Date of admission, September 15, 1918. Civil occupation, shoemaker (cobbler). Habits as to alcohol, good. Family history, negative. Previous personal history, diphtheria fifteen years ago. Venereal history negative. When walking fast becomes very dyspneic and at times has considerable precordial and substernal pain. At night no longer awakens with air hunger, but these pains come at irregular intervals while asleep, awakening him two or three times a night and then going a night or two without them.

Examination. Facies anxious and troubled. Heart dulness apparently normal; nothing noted but a tachycardia. Has some slight tremor; pulse, 80 (sitting); immediately after exercise, 132; two minutes later, 100. Diagnosis: neurocirculatory asthenia.

September 21. Think this man should be put in exercise class for D. A. H. Sent to Disability Board for classification. Classified "C."

GASTRIC ANALYSIS.

	Free acid.	Total acidity.
1	12	33 (30 minutes)
2	29	69 (45 ")
3	41	71 (60 ")
4	45	74 (75 ")
5	50	90 (105 ")
6	43	67 (135 ")

CASE II.—J. B. M., private, 13th Field Artillery, Company C., Field Hospital No. 19. Diagnosis: fracture of the left foot.

Hospital No. 4. Roentgen ray of the left foot by fluoroscope. Unable to see fracture of fibula. Entered Emergency Hospital No. 7, August 3, 1918; foot greatly mangled.

Base Hospital No. 20. Aged thirty years. Race: white. Service, ten years. Birthplace: Illinois. Source of admission: training camp. Occupation: steuplejack. Tropical service: none. Habits as to alcohol: moderate. Family history: negative. Previous personal history: negative. Casualties: none. Venereal history: negative. Fracture of the left foot was caused by a wheel running over the foot. Also contusion of right shoulder. Two roentgen rays taken. Occurred August 2, 1918, about 2 A.M., on the Sergy front.

September 11. Movements of arm are freer and less painful than they were one week ago.

September 19. Cast removed; bones well knitted; foot strapped.

October 30. Is very nervous and at times unable to hold himself.

At night complains of shortness of breath, the result of a cutting pain which starts in the chest and runs down the arm. Is dyspneic upon exertion, also the result of this pain, and becomes dizzy and light-headed. Has a nasal obstruction which seems to cause him much mental worry and adds more symptoms to his neurasthenic mind. Was always a healthy child, but wet the bed when a youngster and was nervous.

Examination. No palatine and corneal reflex. Tremor of hands, coarse: deep reflexes exaggerated. Lungs are clear throughout. Heart sounds are normal; no murmurs; tachycardia. Pulse before exercise, 118; immediately after, 180; two minutes later, 128. Opinion: "In view of this soldier's well-marked neurotic taint, his subjective symptoms, tachycardia and poor response to exercise, believe he has neurocirculatory asthenia. Case quite well marked; will be unable to do first line duty. Should be in D or C class, and should have medical treatment."

GASTRIC ANALYSIS.

	Free acid.	Total acidity.
1	44	73 (30 minutes)
2	59	88 (45 ")
3	61	85 (60 ")
4	75	113 (75 ")
5	87	118 (105 ")

Test for lactic acid, negative. Test for occult blood, negative. Microscopic examination shows nothing remarkable.

RESULTS OF THE GASTRIC ANALYSES. The test-meal, consisting of 100 gm. of bread and a glass of water, was given about 7.30 A.M. on the fasting stomach. At the end of 30 minutes the duodenal tube was passed and approximately 10 c.c. of the gastric contents extracted. A similar amount was then extracted every 15 minutes until 75 minutes had passed (two subsequent extractions followed a half-hour and an hour later). The specimens of gastric contents were promptly titrated for free hydrochloric and total acidity at the end of this time.

The 11 cases of neurocirculatory asthenia showed a uniformly higher acidity average than the control cases. The acidity reached its highest at the end of 105 minutes and fell very slightly at the end of 135 minutes. Likewise the figures at the end of 75 minutes were only somewhat slightly less than the figures of the succeeding period. The average total acidity for these three periods was 83.9, 86.3 and 84.6. The average total acidity of the control cases reached its highest level likewise at the end of 105 minutes but fell sharply in the succeeding half-hour. The figures for the three last periods were 64.5, 67, and 56.6. None of the neurocirculatory asthenia cases showed a low total acidity. The case showing the lowest figures until the last two specimens was still rising when the tube was withdrawn, the total acidity at that time being 80. Of the 11 control

cases all but 2 reached their highest level either 60 or 75 minutes after taking the test-meal. The 2 cases showing the highest total acidity reached their highest level 105 minutes after eating, and so high were their figures that they were sufficient to raise the average of the 11 cases at the end of this period above the average figures of the preceding period.

TABLE I.

6	27	10	38	32	80	96	40	102	38	101
12	33	20	68	20	56	58	28	62	62	67
41	73	59	88	61	71	74	50	90	43	
35	89	46	93	49	85	113	87	118		
41	61	36	93	38	64	105	73	114	69	104
41	95	59	83	45	36	66	33	61	43	79
12	48	18	40	20	50	89	26	88	37	81
0	6	0	12	18	50	70	42	70	48	78
14	42	20	50	16	68	64	60	84	58	80
76	105	55	87	78	103	125	70	98	46	88
	9:27.5	11:35.2	11:09.0	11:14.8	11:51.8	11:54.2	11:54.5	11:09.9	9:13.2	9:76.2
	Av. 30.6	44.4	32.0	40.7	71.4	49.3	49.5	86.3	47.0	84.6

Free hydrochloric acid and total acidity of eleven cases of neurocirculatory asthenia, with average for periods of 30, 45, 60, 75, 105 and 120 minutes after ingestion of test-meal.

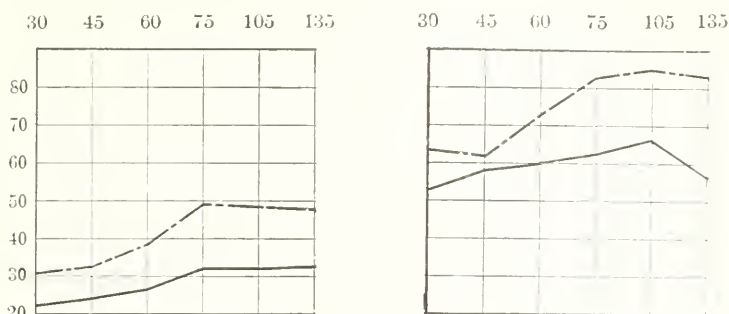
TABLE II.

14	64	10	52	16	64	58	16	34	10	20
12	38	0	22	10	48	20	18	60	20	61
48	76	29	86	26	62	46	22	54	28	40
40	66	50	82	50	76	74	54	72	50	76
40	92	20	34	20	30	35	14	66		
32	57	19	36	31	55	39	28	56	32	47
4	11	48	37	36	68	104	62	104	72	102
28	90	40	77	22	37	37	29	41	26	34
32	75	22	77	25	60	90	45	87	35	60
17	29	30	54	42	69	64	35	48	33	75
	10:23.7	11:28.3	11:03.7	11:03.5	11:06.6	11:37.1	11:34.5	11:07.7	10:32.6	10:50.9
	Av. 23.7	25.7	59.7	28.7	60.5	33.7	31.1	67.0	32.6	35.6

Free hydrochloric acid and total acidity of eleven normal soldiers with average for 1 periods of 30, 45, 60, 75, 105 and 120 minutes after ingestion of test-meal.

The neurocirculatory asthenic cases showed much the same relation in the free hydrochloric figures as was shown in the total acidity; that is, the highest values were reached at the end of 105 minutes—49.5—while the figures for the preceding and succeeding half-hour were respectively 49.3 and 47. With the control cases the free hydrochloric reached its highest level, 33.7, at the end of 75 minutes, the

figures for the preceding period and the last period being 28.7, 31.4 and 32.6 respectively.



Solid lines, normal individuals; broken lines, neurocirculatory asthenia cases.
Chart to left, free HCl; to right, total acidity.

CONCLUSION. In patients suffering with neurocirculatory asthenia there is a very definite increase in the total acidity and free hydrochloric acid as compared with controls. These figures do not represent abnormal hyperacidity. As Rehfuss⁵ has shown that the usual conception of hyperacidity is erroneous, an apparently normal acidity of over 100 is common. They do show, however, that almost uniformly soldiers suffering with neurocirculatory asthenia as contrasted with apparently normal soldiers, both eating the same food, under identical routine and under the same conditions of living, show a higher gastric acidity. This is a diagnostic point which may be of value in differentiating the disorder in questionable cases. It surely seems to add further evidence to that already accumulated that these soldiers are suffering from a neurosis with which is probably associated a hyperirritable vagus.

NEWER CONCEPTIONS OF THE PATHOGENESIS AND TREATMENT OF EMPYEMA.*

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EMPHYEMA is one of the oldest diagnosticable diseases. It was known even to Hippocrates. It cannot be said, however, that its study and treatment have received the precision and refinement

⁵ Possibilities of Fractional Gastric Analysis, Jour. Am. Med. Assn., 1918, lxxi, 1534.

* The Mütter Lecture read before the College of Physicians of Philadelphia, December 12, 1919.

that we would expect from its antiquity. For years the only facts worth knowing about empyema was that it followed pneumonia and that its treatment consisted in that simple formula, "incision and drainage." There was nothing obscure. The pathology and diagnosis were simple, the operation even more simple, so that for decades empyema seemed to offer no opportunity for more intensive investigation. It was more or less a closed subject. Here and there, it is true, an article appeared on empyema, but these concerned themselves mainly with technical modifications of drainage. This state of affairs bred a sense of satisfaction among surgeons in regard to the results of their treatment. The results seemed good enough, and if the results were not better, it was not the fault of the surgeon but of the disease. I confess that I, too, was one of that number, and felt that the mortality was as low as it could possibly be. I remained in this state of exaltation until the year 1914, when at my instigation my adjunct, Dr. A. O. Wilensky,¹ investigated the mortality of empyema at Mount Sinai Hospital for the preceding ten years. To my chagrin and humiliation he found that the mortality reached the formidable figures of 28 per cent. (In partial justification of these figures I may say, in passing, that this mortality includes both adults and infants; of the total of 82 deaths, 53 occurred in infants below three years of age.) This mortality was much higher than my uncorrected sense of values had afforded me and was a rude shock to my complacency. Now this high mortality, I am proud to say, is not distinctive of Mount Sinai Hospital; it is certainly no larger, and in many instances even smaller, than at other hospitals; nor are there any reasons why it should be; the operation and method of treatment was the conventional or standard one practised at every hospital in the country. I therefore suddenly acquired a respect for the disease that I had never felt before, for there are not many operations in surgery that give a mortality of 28 per cent., especially one so commonly performed. I made up my mind then and there that a disease of such formidable mortality demanded investigation, and that is why I welcomed my appointment as one of the surgical members of the Empyema Commission. The conditions under which the commission made their investigations were ideal.

Not only was the attack ably directed from every viewpoint, clinical, bacteriological, pathological, roentgenological, etc., but, and this is important, we were able for the first time to intensively study the disease not only *en masse*, but to witness it, what is so unusual for the surgeon in civil life, from its very inception. As a result of my military experience upon the Empyema Commission at Base Hospital, Camp Lee, General Hospital No. 12, Biltmore, N. C., as chief of the surgical service at Camp McClellan, and later as consultant in the Surgeon-General's Office, my views upon the

pathogenesis and treatment have profoundly altered from those I held while practising civil surgery, and these it is now my privilege to submit to you.

PATHOLOGY AND PATHOGENESIS.

A knowledge of the pathology and pathogenesis of empyema is of fundamental importance in order to understand the principles underlying its treatment. An extensive operative and autopsy experience has helped me to clarify my notions of the pathology of empyema considerably, and has profoundly modified my views concerning the treatment. I shall not enter at great length into the hitherto accepted views concerning the pathogenesis of empyema, except to say that the common understanding hitherto has been that the pleura became infected by contiguity from the inflamed lung. This view did not appeal to me for two reasons: My first objection is that this mode of infection does not occur in any of the other closed serous cavities of the body. Take the peritoneum for instance and its most frequent source of infection, the appendix. Every surgeon with any experience knows that a diffuse peritonitis rarely if ever occurs unless there has been a perforation of this organ, or the walls are so necrosed as to permit of easy transmission of bacteria into the peritoneal cavity. This is likewise true of the hollow viscera of the abdomen. Reasoning by analogy, therefore, it is difficult to see why the pathogenesis of infection of one serous membrane should be different from that of another. My second objection is that infection of the pleura by contiguity would presuppose a direction of the lymph current opposed to that demonstrated and accepted by physiologists and anatomists. To obviate this a double set of lymphatics has been assumed, one passing from the hilum to the pleura, the other passing in the reverse direction. This contention, however, is only a hypothesis and not a fact.

It has seemed to me, therefore, that upon theoretical grounds alone a different pathogenesis than that of contiguity was necessary to explain purulent infections of the pleura, and it has appeared to me to be very probable that gross contaminations of the pleura should occur from a focus in the lung, just as similar infections of the peritoneum occurred. On the constant lookout for such findings, I was not at all surprised, many years ago, to see at autopsy an empyema that had resulted from a rupture of a small subpleural pulmonary abscess. I wondered whether this was not the common rather than the exceptional cause. As operation does not permit of sufficient exposure the demonstration of such a pathogenesis requires autopsy material. This became available *en masse* at Camp Lee, in the spring of 1918, and in a series of perhaps three dozen autopsies we were able to demonstrate in

a great many instances one or more subpleural abscesses, some of which had perforated into the pleura. Additional corroborations of this pathogenesis was furnished by the influenza epidemic at Camp McClellan during my incumbency as chief of the surgical service. Lieut.-Col. E. K. Dunham, who was associated with me on the Empyema Commission, again demonstrated a perforated subpleural abscess in every case of empyema that came to autopsy.

The localization of the empyema depends entirely upon the situation of the ruptured subpleural abscess. If, as is most frequently the case, the empyema is a general or diffuse one the abscess is usually located upon the convex surface of the lung. If the abscess is located in a fissure an interlobar empyema results. When the abscess is on the mesial aspect of the lung we will find retrosternal pus pockets between the lung and the mediastinal pleura. The latter were more common in the earlier streptococcus epidemic than in the later influenza epidemic.

An additional and perhaps obvious proof that ruptured subpleural pulmonary abscesses occur in empyema is the frequent experience that irrigation of empyema cavities with irritating solutions, such as Dakin's solution, results in coughing and choking, showing that communications exist with a bronchus. This perhaps explains why in former years irrigations of empyema cavities with even bland solutions were considered unfeasible. Such communications are furthermore very often demonstrable by bismuth roentgen-ray examinations. I believe these communications exist in every empyema; if small, they heal promptly; if large, they may be the cause of considerable difficulty during the treatment.

I need hardly dilate upon the fact that smaller and larger abscesses occur not only beneath the pleura but also well within the parenchyma of the lung in pneumonias, especially in those of the streptococcal variety. If small they may be absorbed; others rupture into a bronchus; if the infection becomes attenuated they become remediable by operation; usually, particularly if they are multiple, they cause a fatal sepsis. The subpleural varieties offer perhaps the most favorable prognosis, because at worst they form an empyema by rupturing into the pleural cavity. When they do the rapid development of an empyema is, I believe, favored by the presence of the small amount of serous fluid in the pleural cavity, which is present in every case of diffuse pneumonia.

The analogy between infections of the pleura and of the peritoneum is therefore remarkably complete. Unruptured infections within the abdomen also cause serous exudates, which, if uninfected, become absorbed. The one important physiological difference between infections of the pleura and peritoneum is the greater and constant mobility of the lung as compared to the sluggish peristalsis of the intestine, so that adhesions are less liable to form; a free serous pleurisy is therefore the rule.

When now the serous pleurisy is converted into a seropurulent or purulent exudate, encapsulation occurs just as in the peritoneum and is due to a deposit of fibrin on the periphery. The encapsulation also, as in the peritoneum, may be diffuse, localized or multiple. Owing to the recumbent posture the fluid usually collects in the supradiaphragmatic and posterior portions of the thorax, giving rise to the most common form of empyema. Isolated and localized forms, however, are frequent findings and multiple encapsulations are not uncommon.

The important point to remember, especially in reference to treatment, is that, whereas a serous or seropurulent pleurisy is always free, a purulent pleurisy is nearly always encapsulated. The encapsulation may enclose an extensive area, almost the entire pleural cavity, but at some time or another adhesions between the parietal and visceral pleura are nearly always found. An absolutely free empyema, occupying the entire pleural cavity, is, in adults at all events, rarely found.

TREATMENT.

Primarily I wish to emphasize that an empyema in the stage in which frank pus is obtained by aspiration is already an end-product, the terminal event of an infectious process in which the first stage is a pneumonia with a small serous pleurisy, and the second stage a pneumonia with a greater exudation of seropurulent material. The treatment of empyema really begins in the latter stage, so that in this disease, as well as in all acute surgical infections, an early diagnosis is of prime importance. Speaking again in terms of analogy it would be equally as logical to begin the treatment of appendicitis only when an abscess has formed as to initiate the treatment of an empyema only when the exudate has become manifestly purulent. It was not merely the observation of empyemata *en masse*, but the opportunity to witness the development of an empyema from its very incipency that made my military experience in this disease of so much value to me.

I have therefore divided the subject of the treatment of empyema into three stages:

- I. The formative stage.
- II. The acute stage.
- III. The chronic stage.

I. THE FORMATIVE STAGE.

The formative stage of a case of empyema is one of the most interesting phases of the problem. The exact period of its onset can often not be told with precision, because, as already pointed out, every case of pneumonia is accompanied by a certain amount

of serous effusion. As long as the amount is within small limits it does not deserve much attention; in fact, there is very little doubt in my mind that small effusions of a serous nature are usually overlooked.

Furthermore, it also appears to me that early effusions may properly be subdivided into two periods. The first period is merely an evidence of the inflammatory process in the lung and in the greatest majority of instances is moderate in amount. The second period begins with the rupture of the small subpleural pulmonary abscess, which is followed by an intense inflammation of the pleural surfaces and an infection of the fluid, with a very rapid increase in its amount. I have also gained the impression that the amount of the exudate and the rapidity of its accumulation depends to a large extent upon the nature of the infecting organism. Thus I believe, for instance, that the exudates caused by the hemolytic streptococcus, as was seen in the 1917-1918 epidemic, were exceedingly rapid, not only in their formation, but also in their accumulation. I have seen cases of thirty-six to forty-eight hours' duration in which one pleural cavity was filled, and in which reaccumulation was occasionally so rapid that aspiration had to be repeated at twelve-hour intervals. On the other hand the empyemata which followed the later influenza epidemic were slower, both in their formation and reaccumulation.

The patient at this stage is suffering from a number of things, all of which demand appropriate treatment.

1. Of foremost importance is the toxemia, caused by the pulmonary infection, and to a slight degree also by the infected exudate in the pleura. This requires the usual treatment appropriate to the case. In general terms it is what is called "supportive." If successful it serves to tide the patient over the most important phase of the illness.

2. The pneumonia which at this stage of the illness is still in a florid state demands careful attention and appropriate treatment.

3. The large amount of exudate brings in its train a tremendous loss of nitrogen. This observation and its therapeutic importance has been made the subject of an exhaustive study by Captain Richard Bell, of the Empyema Commission.² To replace this loss the patient must be fed on a diet of a high caloric value. Clinical observations have corroborated the great importance of this measure.

4. Of equal importance with the preceding is the presence of the exudate in the pleura. I have purposely avoided the words "infected" exudate because I look upon the mechanical presence of the fluid as of greater importance even than the infection. There can be no excuse whatsoever for overlooking it; particularly in adults, the physical signs of the same are so characteristic that even in the absence of roentgen ray and other instruments of precision it should always be readily diagnosed.

Primarily the patient is suffering from its mechanical presence and this exerts its deleterious effects: (1) By compression of the affected lung (by some this influence is considered beneficial); (2) by pressure upon the mediastinum and compression of the healthy lung; (3) and most of all by pressure upon the heart and consequent kinking of the great vessels. It is for this reason that left-sided exudates are borne less well than those on the right.

To relieve these mechanical effects of large exudates we resorted to the simple device of aspiration with an apparatus that does not permit the entrance of air.

It was truly remarkable to witness the almost immediate benefits of this measure. The patients were more comfortable, the dyspnea was less, the cyanosis was not so marked and the pulse improved in quality. Aspiration was repeated as often as the fluid reaccumulated in sufficient amounts as to demand it; in some instances, especially in the streptococcic form as often as every twelve hours. In a few instances aspirations were even curative.

The question may now be asked why was not an early thoracotomy done? On theoretical grounds such an operation might obviate both the mechanical and toxic effects of the exudate. Practically, however, an early thoracotomy is absolutely contra-indicated, and for the following reasons:

I shall elucidate my argument by first describing the pathogenesis of pleural exudates.

A vertical section of one-half of the normal thorax may be represented as in Fig. 1. As is seen the lung entirely fills the pleural cavity; the parietal and visceral pleuræ are in contact, being separated merely by a very thin layer of fluid.

If an exudate or transudate forms the fluid, being heavier than the air-containing lung, collects in the dependent portions of the pleura and crowds the lung upward and toward the vertebral gutter. This is represented diagrammatically in Fig. 2. This is what usually happens in pleurisy with effusions, in pleural transudates from cardiac or kidney disease, etc.

Suppose now that a subpleural pulmonary abscess ruptures and an early empyema develops. There is a sudden increase in the amount of exudate and a corresponding aggravation of the symptoms.

If a thoracotomy is now performed the fluid suddenly escapes and there is an equally sudden inrush of air, followed by an immediate collapse of the lung. This is illustrated in Fig. 3. The occurrence just related is immediately followed by a fluttering of the as yet uninfiltreated mediastinum, impairing still further the action of the heart. Finally, if the patient survives, the mediastinum becomes fixed with the convexity toward the unaffected side. This condition is represented diagrammatically in Fig. 4. (In parentheses I merely wish to mention that these observations upon pneumothorax apply only to large thoracotomies, and not

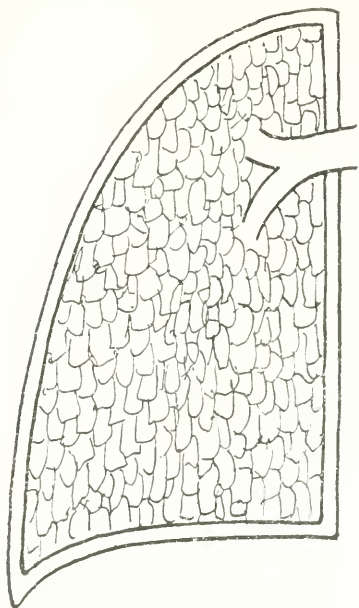


FIG. 1.—Vertical section of one-half of the normal thorax.

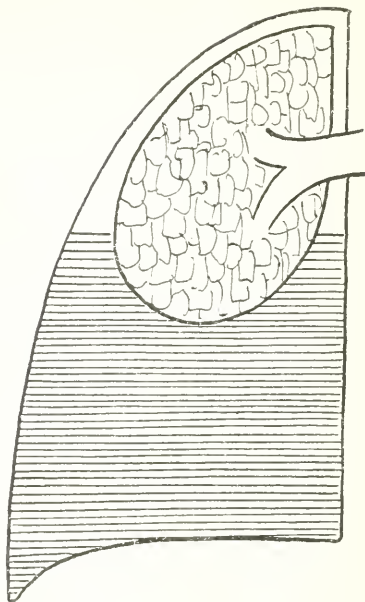


FIG. 2.—Free exudate into pleural cavity.

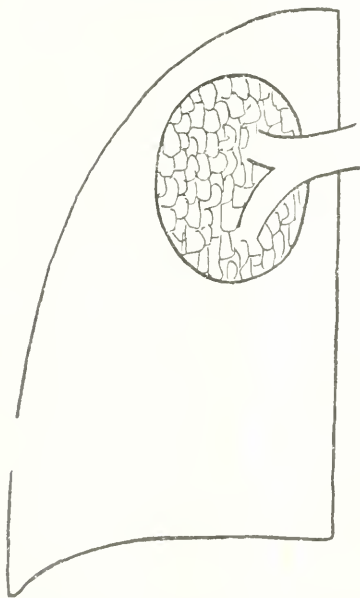


FIG. 3.—Collapse of the lung caused by thoracotomy in the presence of a free pleural exudate.

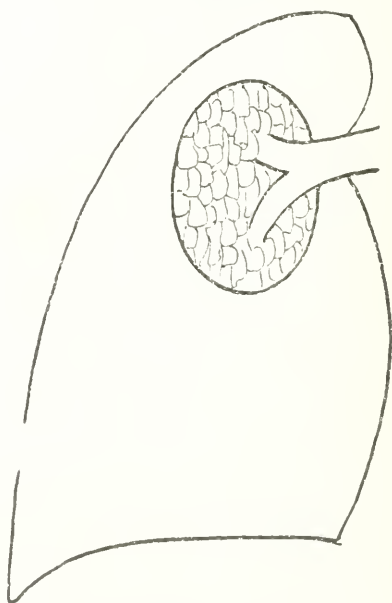


FIG. 4.—Collapse of the lung and fixation of mediastinum toward opposite side caused by thoracotomy in the presence of a free pleural exudate.

to instances in which the opening is of smaller size than the chink of the glottis.) The pathological physiology of pneumothorax has been ably investigated by Garre and Quincke, and by Graham and Bell, of the Empyema Commission.

Theory aside, however, early thoracotomies are attended by a terrible mortality, as the statistics in our military camps during the epidemic of 1917 and 1918 woefully testified. Early operations were probably prompted by the enthusiasm of both internists and surgeons, who for the first time saw empyemata in large numbers develop under their very eye, and felt that early operations, which in other suppurative surgical affections is a great desideratum, would give similarly brilliant results. It was only when frightened by the formidable mortality and a halt was called on early operations that the statistics improved. The patients died not only in large numbers but promptly after the operation. When we consider that these operations were done upon a patient who was at the same time sick unto death with an active pneumonia it is not surprising that the mortality was as large as it is.

Another but less important contra-indication to early operation is the fact that even if the patient survives, the lung becomes fixed in its collapsed position by adhesions, so that a huge empyema cavity results, which takes an interminable time to heal.

To sum up, the treatment of empyema in the formative stage resolves itself to the formula *nil nocere*. The only surgical procedure indicated is frequent aspiration of the chest.

II. TREATMENT OF THE ACUTE STAGE.

When the seropurulent fluid changes into pus, adhesions form between the opposing surfaces of the pleura. A cross-section of the chest in such a condition is represented in Fig. 5. These adhesions are important because they anchor the lung to the parietes. The thorax, therefore, can now be opened without causing complete collapse of the lung. A cross-section of the thorax after opening is represented in Fig. 6. I am speaking now only of the commonest forms of empyema, namely, those situated in the supradiaphragmatic and posterior portion of the chest. Slight variations obviously occur in empyemata in other situations, but the underlying principles remain the same.

I do not know just when these adhesions form; the important point is that I have practically always found them when the chest contains frank pus; so that, I repeat, nearly every empyema is an encapsulated one.

Furthermore, the patient at this time is in a much improved general condition; the pneumonia is over and the general toxemia has subsided. We have nothing to contend against now but the empyema, which causes symptoms from absorption of toxic material

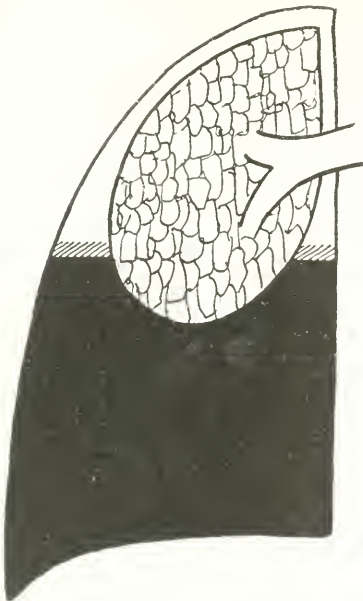


FIG. 5.—Empyema of chest; note adhesions between the visceral and parietal pleura upon the periphery of the exudate.

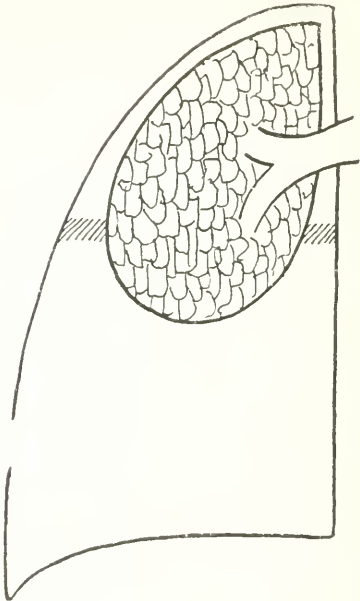


FIG. 6.—Empyema of the chest after thoracotomy; note absence of collapse of lung.

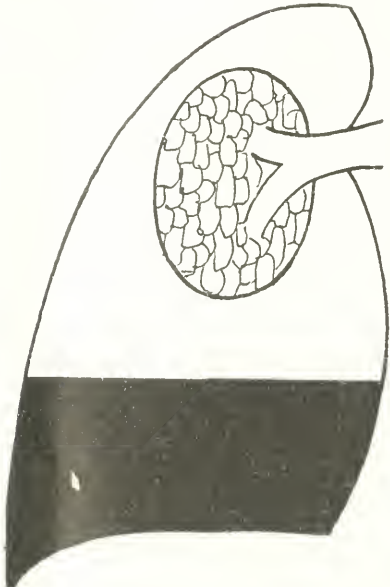


FIG. 7.—Acute pyopneumothorax.

and from the mechanical effects of the fluid alone. The dangers from absorption have, I believe, been hitherto greatly exaggerated, and while I do not advocate needless delay in performing a thoracotomy the necessity for this operation is by no means urgent. Indeed, the only indication for urgent or early thoracotomy is in those exceptional cases in which a pulmonary abscess, directly in communication with a large bronchus, ruptures into the pleura. There is thus formed an acute hydropneumothorax or pyopneumothorax under extreme tension, due to the continuous escape of air into the pleural cavity. The condition is diagrammatically represented in Fig. 7. These patients suffer intensely from dyspnea, and as the lung is already collapsed no harm can be done by an early thoracotomy in order to afford relief.

The operation in the acute stage is one of the safest known. This safety, as already pointed out, is based upon the fact that all around the periphery of the fluid, no matter how large or how small, there is a pyogenic membrane of sufficient firmness to encapsulate it and to convert it into a simple intrapleural abscess. The appropriate treatment is, therefore, that of every abscess, namely, incision and drainage.

In spite of its simplicity each step of the operation requires the greatest punctiliousness. I shall begin with a description of the operation in the commonest form of empyema, namely, that which is located in the supradiaphragmatic and posterior portions of the pleura.

1. ANESTHESIA. All operations on adults and, for that matter, also on older children, can and should be carried out in local anesthesia. The anesthetic of choice is novocain in 1 per cent. solution. The line of the incision is first injected endodermatically, and from this area the deeper tissues are thoroughly infiltrated. It is important to remember that sufficient time should be permitted to elapse to obtain the full effect of the anesthetic. Many a complete failure is due to the neglect of this primary rule; and once the confidence of the patient is lost by failing to obtain the promised analgesia the subsequent steps cannot be properly carried out. I never employ a general anesthetic, and doubt that it is ever indicated, if only care, gentleness and patience are exercised.

2. SIMPLE INTERCOSTAL THORACOTOMY VERSUS COSTATECTOMY. Personally I prefer and advocate in all primary operations for empyema a simple intercostal incision. If critically analyzed the object of the entire operation is to make a liberal incision into the pleura and to insert large enough drainage tubes. I maintain that this object can be obtained fully as well by an incision through an intercostal space as through a retrocostal space obtained by rib resection. I am sure I use tubes as large (to be exact, 40 F.) as the advocates of costatectomy; very often I use even two or more tubes. The advocates of costatectomy claim that the tubes are

kinked unless this is done, but in a great many operations I have never seen such an occurrence and doubt that it can occur.

Costatectomy has the additional disadvantage that in spite of the greatest care the ends of the divided rib very frequently become necrotic and thus become the source of continued suppuration.

Costatectomy, however, is such an ancient and time-honored operation that it is here to stay. I do not deprecate its use; let those who wish it continue to do so. I hold, however, that it is unnecessary.

3. THE SUPERFICIAL INCISION. (a) *The Site of the Incision.* In general the site of the incision depends upon the location of the empyema as guided by the physical and roentgen-ray examination. The incision must fulfil two purposes: (1) It must afford adequate drainage and (2) it must permit appropriate medication of the cavity. The drainage must be free and unobstructed both in the recumbent and erect posture. In the most common location of empyemata, *i. e.*, those which occupy the lower part of the thorax, I prefer an incision in the eighth intercostal space, just behind the posterior axillary line, or at the midscapular line. Theoretical objection might be raised to this location by the fact that the ascent of the diaphragm which occurs in the course of healing of every empyema might cause a kinking of the drainage-tube, but in practice I have never found it to occur.

(b) *The Incision of the Extrapleural Soft Parts.* The cutaneous incision should be of ample length. Two to four inches, depending upon the amount of adipose tissue present; so that with proper retraction all subsequent steps can be carried out under the guidance of the eye. It is important to remember that the incision, if made, as is usually the case, with the arm hyperabducted, will shift when the dependent position of the arm is restored. If this is not considered the surgeon will find that his cutaneous incision is not in alignment with the pleural incision. This is a circumstance which is extremely annoying in the after-treatment, and may require a second incision at right angles to the first. It is readily obviated by outlining the incision while the arm is in the adducted position.

Usually I also excise some of the intercostal muscles. This step has a twofold object: (1) It exposes cleanly the underlying endothoracic fascia and parietal pleura and (2) because the shreds of divided muscle have a tendency to close up the wound and are a hindrance in the after-treatment.

4. THE INCISION OF THE PLEURA. With proper retraction there is now exposed in the bottom of the wound the endothoracic fascia the deep layer of which is lined by the parietal pleura. Both these structures are very sensitive and may be anesthetized additionally by the direct injection of novocain. A small incision is made first and the pus is slowly evacuated; subsequently the incision into the pleura is extended to the full length.

5. DRAINAGE MATERIAL. I use as direct postoperative drainage material a single large sized rubber tube of a rather stiff quality and about one foot long. The tube is forced through a tiny perforation in a piece of rubber dam, approximately four inches square, which is fixed to the tube with a thread at a distance from $2\frac{1}{2}$ to 4 inches from its thoracic end, depending upon the thickness of the chest wall. Near the thoracic end a large fenestra is cut into the tube, so that the fenestra is just inside the pleural cavity (Fig. 8). This must be gauged with some care, in order to permit the rubber dam to be flush with the skin. No sutures are ever employed; on the contrary, both the pleural and external incisions are packed

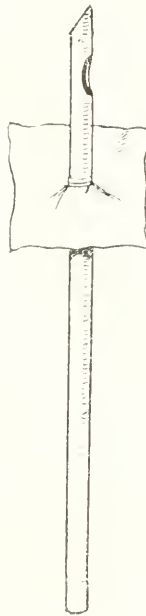


FIG. 8.—Drainage-tube for empyema.

wide open with gauze. The rubber dam is laid smoothly on the skin and its edges are firmly fastened to it by overlapping broad strips of adhesive plaster. A small dressing and a firm binder are applied in such a manner that the long end of the tube (temporarily clamped) finds free egress.

I do not irrigate the cavity upon the operating table, but, as will be seen, I do so promptly upon the return of the patient to his bed. I do not do so from any fear of the irrigation, but merely as a matter of convenience and in order not to prolong the operation unduly.

This matter of irrigation of an empyemic cavity is a very impor-

tant point and deserves careful consideration, as the entire modern treatment of empyema depends upon our ability to do so. If there is anything definitely settled in surgery it is that no empyema should ever be irrigated. There is apparently no valid reason for this strenuous interdiction; as a general rule explanations are given which, if critically examined, will be found not to explain at all. Personally I believe there is a fairly good reason for it, which, however, has not been recognized until now, namely, the frequently found communications between the pleural cavity and the bronchial tree. As already stated, purely for reasons of convenience, I do not irrigate the pleural cavity upon the operating table, but I do so promptly, almost immediately, upon the return of the patient to his bed.

It is greatly to be regretted that even the advocates of the Carrel-Dakin treatment frequently state that certain cases of empyema cannot be treated with Dakin's solution, because it causes an intensely irritating cough; on the other hand the opponents of the method are only too prone to sneeringly discard the entire treatment. As a matter of fact it is not at all necessary, because this irritating cough occurs only when there is a very large open bronchus communicating with the pleura and when the cavity is overdilated with the solution. Experience has taught me that all these patients will tolerate Dakinization perfectly well if administered in the following manner: I usually begin with very small quantities of solution, say 5 c.c. into each tube, and gradually and slowly increase the daily amounts. Under such treatment the pleuropulmonary opening closes in time, and more than that, patients become accustomed to Dakin's solution, until finally they tolerate instillations of full doses.

Upon reaching the ward a simple combination instillation and suction apparatus is attached to the free end of the drainage-tube by means of a T-tube; at a convenient point a second attachment is made for a bottle to receive the discharges (a mixture of pus and Dakin's solution) from the empyema cavity (Fig. 9).

Once an hour, or more or less frequently as indicated, the siphon part of the apparatus is discontinued by clamping; at the same time the instilling apparatus, an ordinary Dakin container, is opened and the requisite amount of Dakin's solution is allowed to run in. After the lapse of five minutes the suction apparatus is reopened and the solution plus secretions is siphoned out. The suction is continued until the next period of instillation.

The advantages of this combination apparatus, consisting of a drainage-tube, which fits air-tight to the chest (in fact is part of the chest wall), instillation apparatus, suction apparatus and receiving bottle are the following:

1. All the discharges are collected into the receiving bottle, and in consequence the wound does not require any change of dressing.

I usually postpone the dressing for eight to ten days, which is as long as the patient is connected with the apparatus.

2. If the operation has been properly carried out the cavity is perfectly dry, and there being no retention of pus, fever does not arise.

3. An early opportunity is given to permit a prompt and efficient use of Dakin's solution.

4. The vacuum created adds to a limited extent in the expansion of the lung. I confess, however, that I do not lay much stress upon the last point.



FIG. 9.—Instillation and suction apparatus.

It is far from me to urge the use of this suction apparatus and I do not consider it in any manner essential. If there be some who do not care to take the trouble with it, or if the hospital personnel be insufficient to devote the necessary time to supervise it, it need not be used. Under such circumstances I would advise the introduction of two drainage-tubes and to pack the wound. Such patients will require an earlier change of dressing.

As is seen the advantages gained from the suction apparatus, as used by me, are not of a fundamental nature. I make this statement with a certain amount of hesitation, because entire systems of treatment have been built up around the principle of a vacuum created by means of suction apparatus. The method originated

as far back as 1891 and was introduced by Billau under the name of "Heberdrainage," but was subsequently abandoned. It was revised and numerous modified in conjunction with Dakin's solution in various army hospitals. *A priori* these methods are very fascinating; regrettably the results, as far as permanency is concerned, are not particularly brilliant.

AFTER-TREATMENT. All patients are dressed only once in twenty-four hours. All the old dressings, including the Carrel tubes and "safety valves" (to be subsequently described) are removed and are replaced by fresh ones. All rules as enunciated by Carrel for the preservation of a perfect asepsis are rigidly adhered to.

The skin for a liberal area around the wound is cleansed, first with a dry cotton sponge, and subsequently with a cotton sponge dipped into benzine. A soft-rubber catheter (25 to 30 F.) is introduced into the cavity, and is connected with a Dakin container. The cavity is thoroughly flushed with Dakin's solution, the patient being turned from the lateral to the prone position, and *vice versa*, until the return flow is perfectly clear.

From one to four Carrel tubes, depending upon the size of the cavity, are now introduced into the cavity; it is the aim to introduce them into various portions of the cavity, though, being done more or less blindly, this is often illusory. In very long and very irregular cavities I have occasionally made use of tubes which were armed with a silver wire stylet. A short drainage-tube, about the thickness of a lead pencil, with one fenestra, guarded by a safety pin, so-called "safety valve," is finally introduced, to permit a free escape of Dakin's solution and secretions.

Right here I might digress for a moment in order to mention that the *rationale* of the entire postoperative treatment must be thoroughly understood. One must not fall into the error of thinking there is something supernatural in Dakin's solution, so far as the cure of an empyema is concerned. All that it can do, or is expected to do, is to sterilize the cavity. It can never supplant good surgery, and the best surgical principle in the treatment of an empyema is good surgery. This is self-evident, and yet I have seen this fundamental principle violated only too often. I have seen innumerable instances in which a single Carrel tube was introduced into the cavity and then Dakin's solution was poured into it; the patients were septic; the withdrawal of the tube was followed literally by the escape of quarts of pus.

I trust it is not necessary for me to reiterate that one of the fundamental prerequisites in the use of Dakin's solution is a good and properly prepared solution; and yet I have seen this rule also frequently violated. As a matter of fact I have found there is no short cut in the Carrel-Dakin treatment, and it is best to follow all directions to their minutest detail. I would go so far as to say, if results are not obtained, it is not the fault of the method but of a faulty application.

The vicinity of the wound is protected, as usually, by sterile vaselin gauze strips. At a distance from the wound the skin is protected from the irritating action of Dakin's solution by the application of Lassar's paste, which was found to be rather more efficacious in this respect than vaselin. As a general rule it may be stated that it is infinitely easier to prevent than to treat Dakin's burns, and it can be very readily done by slight care.

The wound is packed with small gauze sponges moistened with Dakin's solution. A few small fluffs of dry, sterile gauze are placed next to the wound and over that a liberal pad made up of either reclaimed gauze or cotton, which is held in place by a firm binder. The binder should be applied snugly and be provided with shoulder-straps. Nothing is more annoying than a shiftlessly applied binder, as it permits the displacement and loss of tubes and is a source of constant trouble. The Carrel tubes emerge on top of the binder, usually in the vicinity of the shoulder, where they can be readily reached for subsequent instillations.

Definite instructions are given for the instillation of the requisite amount of Dakin's solution; the quantity depends upon the size of the cavity and varies from 25 c.c. to 100 c.c.—in general about one-half of the volume of the cavity—too much cannot be used. It is distributed in equal amounts through all the tubes. Directions also are given as to the intervals between instillations. I have found hourly instillations during the daytime to be most satisfactory; at night the time interval is two hours.

The dressing is not touched for twenty-four hours. It is true the large quantities of Dakin's solution used saturate the dressings pretty thoroughly; but some of it escapes by evaporation, and upon inquiry I did not find that the patients complained of this seemingly annoying drawback.

It is very remarkable, but already at the first dressing the discharge has lost its frankly purulent character. If the case has been properly operated upon, and in the most dependent part of the cavity, the cavity will be found to be perfectly dry, as all the discharges escape through the safety valve. In order to obtain the maximum benefit from the solution, the instillations are given in the recumbent posture with the drainage opening uppermost; even ambulatory patients are ordered to remain in this position for five minutes after each instillation. Exception to the recumbent position is made in cases complicated by large pleuropulmonary fistulæ, as in this position the injected fluid may find its way too readily through the fistula into a bronchus. In almost every one of these patients a position will be found, either prone, or sitting upright, or front, or back, or upon the right or left side in which the instillations are well borne.

It is almost marvelous to see the effect of a properly carried-out treatment. All pus and odor disappear as if by magic. I have

literally dressed one hundred patients, and in all the patients combined not half a teaspoonful of pus was found; in fact, in some cases it was difficult to obtain enough secretions to make a proper culture.

In some of the cases of long standing, *i. e.*, those which have been neglected and in which there was for a long time imperfect drainage, we had an opportunity to watch the character of the discharge. Its consistency was not unlike that of uncooked white of egg, in which there were enmeshed a few grayish particles. With progressive sterilization the discharge lost this appearance and the irrigation was followed by small hemorrhages. We interpreted the first finding as due to the liquefying action of the Dakin solution upon the dense, fibrous deposit upon the pleura, and the subsequent hemorrhages as due to the irritation of pleural granulations.

These slight hemorrhages, which are of no consequence whatsoever, must not be confounded with those occasionally occurring recurrent large hemorrhages, which may be so large as to endanger life. They have been ascribed to the effects of Dakin's solution; as a matter of fact, these accidents have been brought forward as a very powerful argument against the use of Dakin's solution. I am firmly convinced that this is an error. I also have proof that these large hemorrhages are due to an erosion of the intercostal artery, which is caused by the pressure of the drainage tubes. In the slighter cases a firmly applied tamponade may be sufficient to arrest the hemorrhage; in the more severe and in recurrent cases it may become necessary to ligate the vessel.

It is most interesting to follow in cases recently operated upon the changes caused by Dakin's solution upon the infected pleura. When an empyema is operated upon the pleura is found coated throughout by a soft, grayish deposit of varying thickness, composed of fibrin and pus, holding enmeshed myriads of bacteria. As sterilization proceeds this coating disappears very rapidly, exposing a smooth, glistening surface; particularly upon the pulmonary surfaces it is so thin that the underlying lung workings become readily visible and recognizable.

Twice a week smears and cultures are made from the cavity. When very low counts are obtained these are made daily. I place much more reliance upon the cultures than upon the smears; in the latter it is occasionally difficult to differentiate between a bacterium and nuclear debris. As a general rule it may be stated that for every bacterium seen upon a slide about 200 colonies will develop upon a poured plate. When laboratory facilities are not obtainable the counting of bacteria upon a slide may be substituted, however, only with the reservation above mentioned. When sterility is reached the treatment is continued arbitrarily for another week or ten days; at the end of that period all tubes are

left out; in fact, all treatment is discontinued; merely an occlusive dressing is applied. Prompt and permanent healing is the result in many instances, in one case in as short a period as thirteen days. The average time of healing, barring the exceptionally low and exceptionally high periods, which really belong to the chronic stage, is about four weeks.

I have attempted in some cases a plastic closure of the drainage opening, as recommended by the Rockefeller Institute. But the results obtained did not warrant me in continuing this practice. Moreover, I do not see any particular indication for doing so. If the cavity is not sterile a premature closure of the wound is sure to be followed by an infection, with subsequent breaking down of the suture line; if, on the other hand, it is sterile, the wound closes so promptly that even the trivial operation of refreshing and suturing the edges is uncalled for.

Considerable importance is ascribed by most surgeons to the use of blowing bottles in order to encourage the lung to expand. I will not deny that this device helps to a limited degree, but I have also found that most patients, after the enthusiasm of a new toy has worn off, discontinue their use. I have found more benefit from properly carried out light exercises. I encourage particularly light work around the wards, which keeps the patient interested and amused. These exercises are of particular benefit to the myocardium, which, because of the primary toxemia, is always in a debilitated condition.

Patients are encouraged to leave the bed very promptly after the operation. Those that are connected to a siphonage apparatus leave their bed upon the day that the apparatus is discontinued; those that have simple drainage even earlier.

In an earlier part of my paper I have already emphasized the importance of keeping up the nutrition of the patients.

EXCEPTIONAL OPERATIONS.

The operation as just described is applicable particularly in the commonest form of empyema, namely, that the boundaries of which may, roughly speaking, be stated as mesially the lung, laterally the chest wall and inferiorly the diaphragm. An empyema may, however, occur in exceptional locations; as a matter of fact there is no part of the pleural cavity which is immune. The diagnosis of these exceptionally located empyemata, particularly in those of small size, is beset with difficulties. That these exceptionally located empyemata must be operated upon at the place of their location is self-evident; occasionally weird incisions in weird locations must be used. Particularly difficult regions are those in the upper part of the thorax behind the pectoralis major; in these cases I have found it preferable to make a vertical incision,

and to divide the fibers in a transverse direction to the necessary extent. If the muscle is simply retracted it is very probable, that at the termination of the operation the muscle will cover up the drainage opening; a most annoying complication in the after-treatment. I have never seen any drawback from the partial division of the pectoralis major.

Empyemata situated directly in front of the scapula are best reached from the axilla.

Interlobar empyemata are not only difficult to diagnosticate but also difficult to operate. Their diagnosis requires a very careful examination, a knowledge of anatomy and demands particularly a very careful roentgenray study. I am of the opinion that, unless the symptoms are extremely urgent (and, as a rule, they are not), these cases should not be operated upon in haste. A careful differentiation should be made between cases in which the general pleura plus the interlobar pleura is infected and cases in which only the interlobar space is involved. In the former the operation is of no danger; in the latter, particularly if only a small amount of pus is present, and there are no adhesions between the parietal and visceral pleura, it may happen that inadvertently the general pleura is opened with collapse of the lung and infection of the general pleura. It has been my experience that by judicious waiting the interlobar pus collection will increase in size, and when it has come safely near the surface, adhesions will form between the visceral and parietal pleura and the abscess can be opened with perfect safety. It is preferable to operate an interlobar empyema through a costatectomy, as it is important to expose a large surface of the lung, so as to visualize, if possible, the interlobar fissure. The adhesions should then be separated and the abscess drained. Occasionally this cannot be done and the abscess must be evacuated through the parenchyma of the lung. Whenever possible this should be avoided, as it prevents the prompt treatment with Dakin's solution and may give rise to pleuropulmonary fistulae.

BILATERAL EMPYEMA.

Until recently bilateral empyemata have been looked upon as particularly dangerous. It is true that the mortality of these is higher than that of unilateral empyemata, but the reason for the high mortality is not the empyema but the bilaterality of the pneumonia. When the pneumonias have run their course and the case has reached the acute stage of the end-product, empyema, with well walled-off adhesions, neither the condition nor the operation is dangerous. While I would not hesitate, if urgency demanded it, to operate both sides simultaneously (and I have done so) it is preferable to do so at different sittings.

COMPLICATIONS.

Complications of unoperated empyemata are rare. Indeed, it is hardly conceivable that an empyema may have complications except metastatic suppurations. I have seen quite a number of metastatic suppurations, especially in the joints, but, inasmuch as positive blood cultures in empyema are exceedingly rare, I have arrived at the conclusion that such suppurations are rather to be regarded as complications of the malady that gave the empyema than of the empyema itself. I wish to speak especially of one metastatic infection because of its pathogenetic significance. A brain abscess following an empyema is not conceivable on pathological physiological grounds, because there is no way for a thrombus to reach the brain from the pleura. Even, therefore, on purely hypothetical grounds we must assume that if a brain abscess occurs as a complication of empyema there must also be an abscess of the lung, because it is only from such a source that an infective thrombus in the brain may arise.

The complications of a badly treated empyema are legion. The most important is sepsis due to inefficient drainage.

I have already alluded to one of the complications arising from too early operation, namely, the occurrence of enormous cavities. Indeed, I believe that these early operations are more responsible than any other factor for the invention of the multitude of secondary operations.

MORTALITY.

Permit me to quote first a few statistical figures, which a hasty review of the literature, gathered at random, revealed:

Lavrow⁵ figures a mortality of 55 per cent. for all cases, in adults alone 45 per cent. Dunlop⁶ reports a mortality of 36 per cent. in the empyemata in children. Lloyd⁷ reports a very low mortality, namely, that of 20 per cent. Various German clinics quoted by Hahn⁸ report a mortality varying between 8 and 25 per cent. Holt⁹ gives for children under one year a mortality of 73 per cent. and for those under two years a mortality of 58 per cent. Dowd,¹⁰ in a study of 285 cases, 238 of which were children between the age of two and fourteen years, reports a mortality of 25.6 per cent. Lilienthal¹¹ reports the statistics of 95 cases which were operated upon his service at Mt. Sinai Hospital between 1914 and 1917, and shows that he reduced the mortality to 18.9 per cent.

In 299 consecutive cases, collected by Wilensky,¹² from the records of Mt. Sinai Hospital, which occurred between 1904 and 1914, there was a mortality of 28 per cent. In extenuation of this high mortality it is but proper to mention that a large number of these were in infants and that many were in a very poor general

condition, frequently not surviving the simplest operation. (Insertion of a catheter through a trocar.)

Let me furthermore quote from a "report on empyema" which has been rendered to the Surgeon-General of the Army by Major Evarts A. Graham and which he has compiled from the replies to a questionnaire transmitted from the principal Base and General Hospitals.

"The average mortality based on the replies from 25 camps, which gave their results is 30.2 per cent. But this mortality, as high as it is, does not begin to represent the remarkably high mortality which has occurred in some of those camps which had a large number of cases. For example, at Camp Funston, in 85 cases of empyema the mortality has been as high as 84 per cent. Again at Camp Greene, in 92 cases of empyema, it has been 53.2 per cent.; at Doniphan it has been 57 per cent. and at Wheeler, 65 per cent."

Continuing further Graham says: "Possible explanations of the striking differences in mortality reported from various camps in the empyema cases are to be found: (1) In the fact that there has been a marked disagreement concerning what cases should be considered as empyema, and (2) in the method of treatment employed.

"Owing to the fact that the exudate most commonly found is a slightly turbid serofibrinous fluid, with pus demonstrable only microscopically, in some of the camps only those cases have been considered as empyema which yielded frank macroscopic pus. In general, those camps which reported the lowest mortality have regarded as cases of empyema only those in which the exudate has been frank pus; and conversely the highest mortality figures have come from those camps in which all cases showing even microscopic pus in the pleural exudates have been considered as cases of empyema."

I have quoted above the mortality statistics taken at random from a number of observers. On the other hand, conversations upon the subject with colleagues in various parts of the country almost universally elicited the reply that their mortality in empyema was very low. When asked to study their figures they confessed to a mortality of respectable dimensions. I have gained the impression that the mortality percentage gained from actual statistics is high while the mortality percentages quoted from memory is low.

In spite of the very high mortality quoted I have arrived at the conclusion that empyema as such has a very low mortality. I would even go so far as to say that empyema should have no mortality. When a patient dies with an empyema in the acute stage the cause of death is not the empyema but the pneumonia which caused it. A striking evidence of this is seen in cases of undiagnos-

ticated empyema; at autopsy there is always found a pneumonia in the fullest bloom. If the late operation is done, *i. e.*, when the pneumonia has run its course, the operation is perfectly simple and even patients in a greatly debilitated condition stand it with ease and safety.

That a badly treated empyema has a mortality goes without saying, but mortality percentages presume proper treatment. If such a patient dies, the cause of death should not be ascribed to the empyema but to the bad treatment.

III. TREATMENT OF CHRONIC EMPYEMA.

In view of the experiences which I have gained, particularly during the last two years, I have a certain diffidence in defining the word "chronic," as it bears upon a case of empyema. Formerly a case of empyema was considered chronic, which did not heal or which lasted a long time, and which usually required at least one secondary operation for healing. I do not consider this definition a very happy one for reasons which will become apparent.

My conception regarding the manner in which an empyema heals has undergone a very radical change since my recent experience. Formerly I was under the impression that an empyema healed in only one way, namely, by a process of obliteration, which in turn was caused by a gradual expansion of the lung, and by the formation of adhesions between the visceral and parietal pleura. Only when the entire affected pleural surfaces became adherent did the drainage opening close. This is the only method of healing that was known up to two or three years ago and may for that reason be called the "classical method." It has been stated that a properly drained empyema, even without the use of any antiseptics, sterilizes itself, but I have never found this to be the case; on the contrary I found numerous bacteria up to the very moment of final closure. When the cavity persisted I observed that the drainage opening did not show the slightest tendency to close; on the contrary, in spite of earnest prayers, and perhaps extensive operations, it failed to close in many instances.

During the past three years the following variations in the method of healing of an empyema have been scientifically established:

1. The far-reaching observations at the War Demonstration Hospital of the Rockefeller Institute have taught us that empyema cavities can be rendered bacteriologically sterile by means of the Carrel-Dakin treatment, and when sterile the drainage opening can be closed by secondary suture. According to the reports from the Rockefeller Institute a definite cure results in about 75 per cent. of the cases. Personally I believe that recurrence follows in a certain percentage of these cured cases; but there is no denying

that a real cure follows in some cases. I am not aware that the method of healing has as yet been described in detail by the originators of the method. My own observations in a few cases have led me to the conclusion that the cavity heals by the absorption of the sterile exudate that fills the cavity after closure of the wound.

2. During my stay at General Hospital No. 12 I had an experience which threw a flood of light upon my speculations as to the closure of empyemata. An empyema treated by the Carrel-Dakin method had been finally allowed to heal. About one month after healing my colleague upon the Empyema Commission, Dr. Franklin A. Stevens, found upon routine physical examination, which was verified subsequently by roentgen-ray examination that the patient had a definite pneumothorax. I watched this case with great interest and care. An occurrence of this character was unknown to me, and I confidently looked forward to a reaccumulation of the pus. The unexpected, however, happened. Not only did no reaccumulation occur, but the pneumothorax disappeared and was replaced by the expanding lung.

3. The occurrence in the case just related made me think very hard. It gave me the clue that I needed. Whereas up to that time operations upon cases of chronic empyema were of almost daily occurrence with me, I immediately ceased all further operating, and merely proceeded with the intensive sterilization of the cavity. When sterilization was complete all treatment was discontinued and the outer wound was allowed to close. Subsequent examinations showed that the healing occurred through the intermediary stage of a pneumothorax, as in the case just related.

There are therefore in addition to the "classical" method at least two other methods of healing of empyema. It is on this account that I now find difficulty in defining the word "chronic" as it relates to empyema; but in the light of our present knowledge I would exclude from the chronic group any case of empyema which is amenable to sterilization by means of the Carrel-Dakin treatment.

If the cases of empyema which cannot be remedied by even long-continued treatment with Dakin's solution are examined there will always be found a definite underlying cause the removal or eradication of which, occasionally by a very trivial operation, will lead to successful issue. These reasons are not very numerous, viz.:

1. *Cases in Which Drainage Opening is not Dependent.* In the commonest form of empyema, namely, that located in the postero-inferior part of the thorax, almost any opening into the chest situated posterior to the midaxillary line is dependent as long as the patient is in a recumbent posture. If, however, the drainage opening has been placed too high, trouble promptly ensues, when the patient assumes the erect posture, because a chance is given for the formation of an undrained or poorly drained part below

the drainage opening. The establishment of a second drainage opening in the dependent position will promptly remedy the error.

2. *Cases with Contracted Drainage Opening.* It is surprising how many cases of empyema are allowed to drift into a state of chronicity on account of the neglect of this very obvious fault. They formed a very large percentage of the cases in the military service. In the treatment as advocated by me for all cases of empyema an adequate opening is a most important element, not only for the purpose of drainage but also to permit a proper sterilization of the cavity. The drainage opening should permit the easy introduction of at least one good-sized drainage tube, and, depending upon the size of the cavity, from two to six Carrel tubes. The treatment of cases of chronic empyema due to a contracted drainage opening depends upon whether or not this opening can be dilated sufficiently by the introduction of increasingly larger and larger drainage tubes. If this is possible that is all that is necessary; if it is impossible, because of the reformation of the previously resected rib, it is advisable to again excise the rib.

3. *Cases with Necrotic Ribs.* This is a very frequent cause for our inability to sterilize the empyema cavity. The researches of Blake have definitely proved that the interstices and the Haversian canals of sequestra teem with bacteria, and in consequence the Dakin solution never reaches these bacteria. The result is that the empyemic cavity is becoming continuously reinfected. The treatment is self-evident, namely, removal of the sequestra or necrotic ends of the ribs.

4. *Cases with Retained Foreign Bodies.* These form a large percentage (13 per cent.) of the cases that cannot be sterilized by the Carrel-Dakin treatment. The variety of foreign bodies which has been lost in an empyema cavity is unlimited. The most frequent is drainage tubes, including Carrel tubes. Other foreign bodies that I have found were gauze sponges, tampons, rubber dam, large loose sequestra, etc. The diagnosis of rubber tubes should be readily made with the roentgen rays; yet it is surprising that even they may be overlooked.

5. *Cases with Side Pockets and Lateral Branch Sinuses.* The formation of these is a rather interesting problem and may occur in one of several ways. Usually the adhesions in empyema form in a more or less regular line around the periphery of the exudate; sometimes, however, the adhesions form in an irregular manner, so that lateral pockets form which drain through a small opening into the main cavity; after a while these pockets contract, forming tortuous lateral sinuses.

Occasionally it happens that the adhesions form in such a peculiar manner that we are dealing from the very outset with two separate empyemic cavities, separated by a wall of adhesions. In a majority of cases the adhesions are so firm that the two cavities

remain separate for an indefinite time. In some instances the smaller cavity ruptures into the main cavity and makes a communication which is usually inadequate for drainage and treatment.

Finally, irregular cicatricial contractions may occur in the wall of a sinus, which has drained for a long time, thereby shutting off a portion of the sinus, forming a sort of irregular figure of 8.

The reason why these cavities do not heal is simple; they are impossible of sterilization by the Carrel-Dakin method. In their treatment an accurate diagnosis of their location and extent is of prime importance; this can be very readily done by means of the roentgen ray after injecting an opaque substance. Such side pockets should be opened (usually by costatectomy) and sterilized independently of the main cavity. When this is impossible, their exposure through a large intercostal incision by way of the main cavity is indicated.

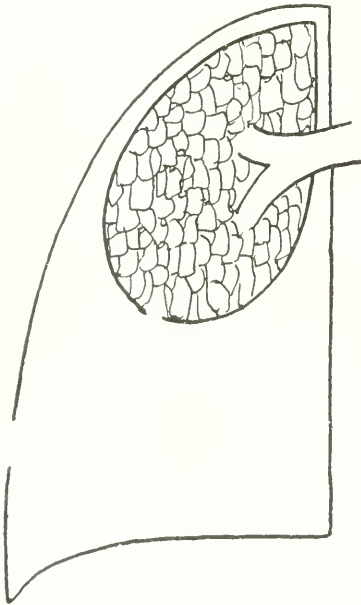


FIG. 10.—Pleuropulmonary fistula.

6. *Pulmonary Fistula.* The etiology of these has already been discussed in detail in the chapter on pathogenesis. When the abscess causing the empyema is small, the perforation usually closes early, so that the injection of Dakin's solution may be carried out without causing disagreeable by-effects.

If there is a communication of the abscess with a bronchus of larger size, we obtain the not infrequent complication known as "pleuropulmonary fistula" (Fig. 10). In the presence of this lesion distention of the cavity with large quantities of Dakin's solution

causes a very distressing cough. Such patients, however, stand the instillations of smaller amounts with perfect comfort, more particularly if attention is paid to the posture of the patient, while the fluid is instilled. A position will nearly always be found in which the instillations do not cause distress. In rare instances the fistula is of unusual size, varying in diameter from that of a pencil to a little finger.

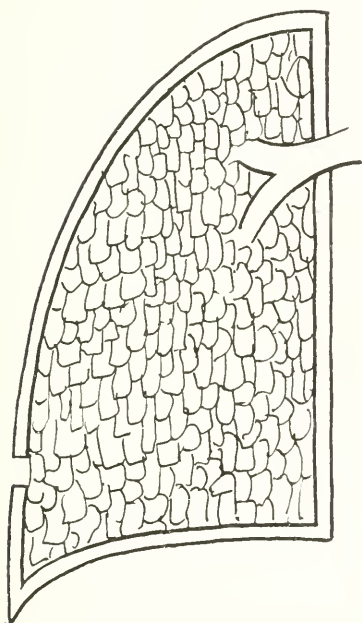


FIG. 11.—Bronchocutaneous fistula.



FIG. 12.—Residual empyema.

Finally it may happen in some cases of empyema, particularly those that have drained for a long time, that the lung has expanded until it fills the entire pleural cavity. In such instances the opening into the lung may become adherent to the drainage opening. There is formed a short channel, leading directly from the skin into a bronchus. On coughing air a slight amount of bronchial mucus is expressed. A sinus of this description should be called "bronchocutaneous fistula." They are exceedingly difficult, if not impossible, to cure without operation, because the bronchial and cutaneous epithelium become continuous and form a so-called "lip fistula." In rare instances I have succeeded in curing these fistulae by a thorough cauterization of the tract with a fine Paquelin cautery. Formerly I have practised extensive operations upon these cases, the operation consisting in an extensive thoracoplasty followed by extirpation and suture of the sinus. I believe, however, that in

most instances this is not necessary. Satisfactory results are obtained by mobilizing the lung and excising the sinus. Thereby converting the bronchocutaneous fistula into a pleuropulmonary fistula. Subsequent healing is not, as a rule, protracted; an inversion suture of the fistulous opening in the lung may shorten the period of healing.

RECURRENCES.

The question of recurrences is intimately connected with that of chronic empyema; in fact, a chronic empyema may well be defined as one which has a tendency to recur.

If we analyze the physical forces which enter into the healing of an empyema we will find that they are composed of several factors, all of which tend to diminish the thoracic cavity. They are: (1) The ascent of the diaphragm, (2) the direction of the ribs becomes more vertical, (3) the intercostal spaces become narrower, and (4) the arc of the ribs approaches closer to the median line. At the same time the lung expands until the parietal and visceral pleura become adherent. It is only when this stage has been reached that we can speak with any degree of certainty about a cure; whenever a space is left there is always the possibility of a recurrence. Broadly speaking, therefore, these reaccumulations are always a reflection upon the method of treatment, for usually they mean that drainage and antiseptic treatment of the cavity have been discontinued prematurely. I have found that this contingency is particularly liable to occur if the external incision is closed operatively, because it not infrequently happens that good judgment is supplanted by haste. Even the strictest precautions, such as smears and bacteriological cultures, do not always furnish a reliable guide to the presence or absence of microorganisms. It again only proves the value of the well-recognized axiom in medicine, that a negative proof is no proof.

An excellent resumé of the recurrences in empyema has been compiled by Dr. Franklin A. Stevens.¹³ Stevens shows that recurrences are less frequent after the Carrel-Dakin treatment, as proved by the following figures.

1. Healed without Carrel-Dakin treatment	56
Recurrences	10 = 18 per cent.
2. Healed with Carrel-Dakin treatment	63
Recurrences	3 = 4.7 per cent.

The diagnosis of recurrent empyemata is difficult if the signs and symptoms are not marked. Examinations with the roentgen ray, especially stereoscopically¹ are of prime help.

The treatment of recurrent empyema differs in no wise from that of an ordinary empyema. Owing to a narrowing of the intercostal spaces it is usually preferable in recurrent cases to resect a rib.

RESIDUAL EMPYEMATA.

Many observers group residual empyemata with the recurrent empyemata; this is erroneous, because of essential differences in their pathogenesis.

Residual empyema is the result of an irregular and multilocular encapsulation during the formative stage of the empyema. At the primary operation, as a rule, the smaller of the two cavities is overlooked, so that only the larger is drained. Sooner or later the patient does not do as well as he should, and upon physical examination, sometimes even long after the main cavity is healed, another pus focus is found.

The diagnosis of the existence and location of these residual empyemata is exceedingly difficult, particularly if they are of small size. There are two symptoms which should lead one to suspect a residual empyema: (1) A recurrent or daily evening fever, and (2) perhaps even a more important symptom, the fact that the patients do not regain their normal weight no matter how liberally fed.

It is the fear of these residual abscesses which lead some surgeons to advocate a wide operation for all primary empyemata, exploring the entire chest, and breaking up all adhesions and septa. I cannot concur in this opinion, as I deem it preferable to do two comparatively trivial and safe operations to one large and hazardous one. Furthermore, the occurrence of residual empyema is too rare to justify such extensive and formidable primary operations.

Occasionally the second pus focus breaks through into the primary cavity; usually a second operation is necessary. If a residual empyema has not been discovered until sometime after the primary operation a costatectomy is indicated, because of the narrowing of the intercostal spaces. In the cases in which the existence of the second pus focus is known at the primary operation, and in these the term of "multilocular empyema" is more applicable, an intercostal incision is all that is necessary.

CHRONIC EMPYEMA SINUS.

Custom makes a very definite distinction between these and the previously discussed cases of chronic empyema. There is in reality no difference, as it is merely a question of degree. Some cases of chronic empyema have a large cavity and a short sinus; others have a long sinus and a small cavity. Special operative procedures in large numbers have been described for their cure, most of which, to my mind, without any particular justification. I believe what I have said of the treatment of chronic empyema in general applies to that of the chronic sinus as well.

OPERATIVE PROCEDURES IN CHRONIC EMPYEMA.

In spite of the best of care some cases of empyema will not heal. I have no hesitancy in stating, however, that if the treatment of the acute and chronic stage is carried out along the lines laid down in previous portions of my paper their number will be infinitesimal as compared to former years. It is in these cases, and in these cases only, that recourse must be had to one of the major operations so called.

The major operations (and I use the word major deliberately, because not one of the originators of the method will confess to really "major" character of his operation) can be divided into two main groups:

I. *The operations which aim to obliterate the empyemic cavity by collapsing the chest wall.* (Estlander, Schede, Quenu, Beck.)

1. Estlander's¹⁴ operation aims at an extirpation of that part of the bony chest wall which overlies the empyemic cavity. The soft parts of the chest wall are then packed down into the cavity against the visceral pleura. The method is applicable only in cavities of limited extent.

2. The Schede¹⁵ operation is decidedly more extensive, but is applicable in cases of total empyema. It follows, therefore, that in comparison with the preceding the Schede operation is one of magnitude and should by no means be lightly undertaken.

3. The Quenu operation is only a modification of the Estlander operation, which it is supposed to supplant. In this operation the ribs overlying the cavity are not removed but are divided at two ends of the incision, so that instead of having a flap made up only of soft tissues the flap is made up of soft tissues plus mobilized ribs. The entire flap is then depressed so that it comes into contact with the visceral pleura.

4. Beck¹⁶ reports very satisfactory results from his "flap-sliding operation." I cannot, however, even after a careful reading of his publication, see wherein this operation differs materially from the Estlander unless it is in the cutaneous incision; and all writers after Estlander, and even Estlander himself, have already deviated from his original incision; in fact, it is recommended that this be done.

II. *The operations which aim at a reëxpansion of the lung by liberating it from the heavy, more or less organized, fibrous deposit, which confines the lung, and prevents its expansion.* (Delorme, Fowler, Lilienthal, Ransohoff.)

1. The Delorme¹⁷-Fowler¹⁸ operation aims at a reëxpansion of the lung by removing the fibrous deposit which covers and confines the lung. Unfortunately the operation does not always succeed: (1) Because the peeling away is exceedingly difficult, if not impossible, so that numerous perforations are made into the parenchyma of

the lung; and (2) because in cases of long duration the lung itself is already fibrosed to such an extent that it no longer expands.

2. The Lilienthal^{19 20} operation aims at a similar objective. This operation is a decided improvement upon the former, because it is not near as formidable. Lilienthal has conclusively demonstrated that with the aid of a good rib spreader the entire operation can be done through a long intercostal incision, with the possible added rapid temporary division of one or two ribs near their angle.

3. Ransohoff²¹ attempts to overcome the not infrequently found difficulty of not being able to peel back the fibrous deposit by merely making innumerable incisions into it in criss-cross fashion.

It is exceedingly difficult to give an absolute indication as to the choice between these operations. Personally I am of the opinion that all of them have a very definite, though in the light of my present knowledge, a much more limited indication than was formerly thought to be the case. At the present moment I am more inclined to favor the lung expanding operations over the chest collapsing operations: (1) Because they are much more conservative of lung function, and (2) because they are followed by less deformity. In a certain number of cases good results will be obtained from the combination of the two methods.

All these operations have a very definite mortality. The Estlander operation has the lowest mortality (about 15 per cent.), but the real indications for this operation are limited. The Schede operation has the highest primary mortality (over 20 per cent.). The definite cures in all vary between 50 and 60 per cent. The remainder makes up the deaths, improvements and failures.

In my military service, before I found that I could heal chronic empyemata by simpler methods, I performed a number of Schede and Estlander as well as Delorme operations; all of my patients were in such excellent physical condition by the time they came to operation, with absolutely sterile cavities, that I did not have a single fatal issue. In passing I may mention that I have found the decortication operation particularly difficult in the empyemata caused by the hemolytic streptococcus. Of late, again, more frequent recourse is had to the decortication operation in the military service and, I am given to understand, with very gratifying results.

As is seen I place the indications for these operations quite differently than I did in my previous communications²² upon the subject. Formerly I was much more radical in my views and I recommended extensive operations in cases which I know now would heal without any operation.

BISMUTH PASTE TREATMENT OF EMPYEMA.

The treatment of chronic empyemata with the injection of Beck's bismuth paste is deserving of special consideration. The

method comes very highly recommended not only from its originator but also from other surgeons. I also have used it and was particularly careful to follow all instructions; regrettably, however, my results were not very encouraging. In a few instances, it is true, healing followed very promptly, but the cure was only of limited duration, because practically all of the cases were followed by a recurrence, extrusion of the bismuth paste and continuance of the suppuration. An additional and important drawback of the method is that, in spite of all precautions to obtain pure chemicals, it is occasionally followed by toxic symptoms; a number of these cases were encountered in the military service. Beck advises the injection of warm olive oil for the removal of the bismuth paste, but I have not found this to be very efficacious, more particularly when the channel or cavity is very tortuous.

CONCLUSIONS.

1. Empyema in most instances results from the rupture of a small subpleural pulmonary abscess.

2. An empyema is the final stage of a process in which the first stage is a serous pleurisy and the second a seropurulent pleurisy. The latter is the so-called "formative" stage of an empyema.

3. The "formative" stage is unaccompanied by pleural adhesions. The stage of final empyema is always accompanied by adhesions.

4. The vast majority of empyemata are of the encapsulated variety. Very few occupy the entire pleural space.

5. Metastatic suppurations accompanying empyema are to be found rather as complications of the causative pneumonia than of the empyema.

6. The treatment of an empyema should be begun in the formative stage before the exudate has been converted into frank pus.

7. It is unwise to perform an operation in the formative stage. The mortality is terrific because the accompanying pneumonia is still in full bloom, and, furthermore, because of the absence of adhesions there occurs a pneumothorax with "fluttering of the mediastinum" and consequent embarrassment of the heart action.

8. The best surgical procedure in the formative stage is repeated aspirations, done every twelve to twenty-four hours, in order to relieve the respiratory embarrassment due to the mechanical pressure of the rapidly accumulating fluid. In a few cases this measure is curative.

9. Feeding with a diet rich in calories is an important adjuvant in the treatment of the formative stage.

10. The treatment in the acute stage of an empyema consists in a simple intercostal thoracotomy. This operation need not be considered an urgent one, and should be performed when the

patient's condition is otherwise perfectly satisfactory. This is the so-called "late" operation.

11. Urgent thoracotomy is indicated only in acute pyopneumothorax.

12. The Carrel-Dakin treatment, properly carried out, has proved of superlative value in the postoperative treatment of empyema and should be used in every case. There are no contraindications to its use.

13. The mortality of acute empyema by these methods is lower than that reported by other methods of treatment.

14. Empyema cavities heal by three methods: (a) By the formation and absorption of a sterile exudate; (b) by the formation and "absorption" of a closed pneumothorax; (c) by the "classical" method, *i. e.*, the expansion of the lung and obliteration of the pleural cavity by adhesions.

15. Chronic empyema should not occur, or at least should become very rare, if the methods of treatment of acute empyema as formulated above are practised.

16. "Chronic" cases of empyema may be defined as such which are not amenable to treatment by the Carrel-Dakin method.

17. Recurrences in empyema are usually the result of undue haste. The percentages of recurrences is less after the Carrel-Dakin method of treatment than after any other.

18. The vast majority of operations that have been devised for chronic empyema will have a very limited field of usefulness if the methods of treatment advocated above are carried out.

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OBSERVATIONS ON RHEUMATIC FEVER AT UNITED STATES BASE HOSPITAL NO. 6, A. E. F., IN THE SPRING OF 1918.

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IN the spring of 1918 the soldiers admitted to U. S. Base Hospital No. 6 with rheumatic fever were sent to special wards for observation by one medical officer. Between the middle of February and the middle of June 73 such patients came under my observation in this way. The records of this series of cases brought out points of interest. The following table summarizes the findings:

HISTORY.

	Cases.	Per cent.
Previous history of rheumatic fever	37	51
Doubtful previous history of rheumatic fever	3	4
Previous history of chorea	2	3
Previous history of scarlet fever (four of these cases had scarlet fever recently)	7	10
Previous history of tonsillitis	30	41

EXAMINATION.

Tonsils, large or ragged	29	40
Tonsils, previously removed	3	
Tonsils partially removed	1	
Joints involved:		
Knee	62	85
Ankle	43	59
Shoulder	33	45
Wrist	27	37
Foot	25	34
Elbow	22	30
Hand	20	27
Hip	20	27

COMPLICATIONS.

Acute pericarditis (two of these cases showed evidence of fluid; one was tapped and 300 c.c. removed)	7	10
Acute pleuritis (left-sided, 6; right-sided, 8; one showed fluid)	14	19
Valve involvements:		
Mitral	29	40
Mitral and aortic	6	8
Tricuspid	1	1
(Nearly all of these cases showed chronic valve damage. There were a few acute changes followed, the murmurs varying in intensity and quality from day to day.)		
Acute heart-block	3	4
Purpura	3	4
Streptococcus septicemia (proved by blood culture)	3	14
Deaths	2	3

of 21 cases
cultured.

DATE OF ADMISSION.

	Cases.
February	8
March	22
April	18
May	17
June	4

Of the 3 cases with streptococcus septicemia 2 recovered and were discharged to full active duty two months after the positive streptococcus cultures were obtained. The heart of the one was apparently uninvolved; in the other a diagnosis of tricuspid endocarditis was made. The third case died in the United States after a protracted illness of many months.

In another soldier, Frontisi, twenty-five years old, a very remarkable recovery took place after a five months' illness, beginning with acute polyarthrititis and continuing with septicemia, marked mitral endocarditis, frequent embolism (leg, arm, abdomen) and severe anemia. At the height of the illness, ten weeks after the onset, the red blood corpuscles numbered 2,400,000 per c.mm. and the hemoglobin was 47 per cent. (Sahli). The white count ranged between 8000 and 15,000. Six weeks after the low red count convalescence had become well established, the red count then being 4,900,000.

Osler in discussing rheumatic fever states that at the Johns Hopkins Hospital, Baltimore, Maryland, for the fifteen years ending 1904 there were 330 cases of rheumatic fever, with 9 deaths (2.7 per cent.).¹ In London the disease seemed commonest in September and October, and at the Montreal General Hospital and in Baltimore the largest number of cases were admitted in February, March and April. The order of frequency of involvement of the joints in Osler's series was knee, ankle, shoulder, wrist, elbow, hip, hand and foot. The average leukocyte count was 12,000 to the cubic millimeter. Thirty-five per cent. of Osler's cases showed organic valve lesions: in 96 per cent., the mitral; in 27 per cent., the aortic; in 23 per cent., the lesions were combined. Pericarditis was present in 20 of the cases of Osler's series, or 6 per cent.; in only 4 was there effusion. Osler advises the salicylates, 15 to 20 gr., every one to three hours, until the pain is relieved. He states that "there can be no question as to their efficacy in relieving the pain. Some observers consider that they also protect the heart, shorten the course and render relapse less likely."

The most striking lesson learned from the series of cases of acute rheumatic fever at U. S. Base Hospital No. 6 was the remarkable response to forced salicylate therapy. Almost invariably there was an abrupt ending of joint pain, swelling, fever and malaise. At one time there were two wards full of cases of rheumatic fever. We gave the salicylates in large doses to the patients in one ward.

¹ Osler, William: Principles and Practice of Medicine, 1912, 8th edition, p. 372.

That was their only therapy, except for good nursing care. These patients did wonderfully well. The other patients in the other ward were given no salicylates internally at first, but received oil of gaultheria and camphorated oil applications to their joints and phenacetin and veronal by mouth. Their pain and discomfort was dulled to a slight degree, but after two or three days of suffering the salicylates were given to them also in large doses, with striking and rapid relief. Aspirin and sodium salicylate were used, almost always aspirin. The routine procedure in the acute cases was the administration by mouth of 30 gr. of aspirin every four hours until the symptoms were relieved; usually 200 to 300 gr. were necessary in the course of two or three days to bring complete relief. After that the drug was continued in small doses, 10 gr. two or three times daily, for example, for a week or as long as seemed necessary. Toxic symptoms were astonishingly rare. No alkali was given, the aspirin being tolerated easily by the gastro-intestinal tract. Only 3 or 4 cases of the entire group failed to be checked by the salicylate and continued in their illness for a fortnight or more. Patients, as a rule, had been sick two or three weeks before admission to the hospital. They remained in the hospital usually about three weeks before being discharged to duty. A few with cardiac complication were returned to the United States.

SUMMARY. 1. In a series of 73 soldiers with acute rheumatic fever, 51 per cent. gave a previous history of rheumatic fever and 40 per cent. showed large or ragged tonsils.

2. The joints involved in order of frequency were knee, ankle, shoulder, wrist, foot, elbow, hand and hip.

3. Acute pericarditis was found in 10 per cent. of the cases, usually very transient. Acute pleuritis was found in 19 per cent.

4. There was evidence of mitral endocarditis in 40 per cent. of the cases; mitral and aortic endocarditis combined in 8 per cent. Most of these cases were apparently of long standing. Acute temporary heart-block was discovered in 4 per cent. of the cases.

5. Three cases made striking recoveries after a very serious prognosis had been given. In two of the three streptococcus septicemia was found by blood culture; both of these soldiers returned to full active duty two months later. The third case, although suffering from serious permanent heart trouble, survived a long rheumatic infection complicated by frequent embolism and by a severe anemia, the red corpuscle count falling as low as 2,400,000 per c.mm.

6. Response to forced salicylate therapy was very striking. It seemed that the course of the disease was shortened by salicylates.

It is probable that salicylate therapy when forced in rheumatic fever acts as prophylaxis against cardiac involvement by shortening the disease.

STUDIES OF THE PRENATAL TRANSMISSION OF SYPHILIS.¹ I. SYPHILIS OF THE TESTICLE.

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THE testicle is one of the most important organs in the body to become involved in syphilis. In all probability there exists an intimate relationship between such an involvement and the transmission of the disease to the spouse and progeny of the infected individual. Moreover, involvement of this organ is of more than passing interest to the experimental research worker in syphilis, to the pathologist, to the surgeon and to the clinician.

The testicle in animals is particularly susceptible to experimental infection with syphilis. In Neisser's² experiments with apes and monkeys the testicles of infected animals always proved to be infectious even when inoculations with the spleen and bone-marrow failed. This investigator states, "It appeared that the testicles acted particularly well and long as a depot of the virus." Testicular inoculations in rabbits with the *Treponema pallidum* produce a high percentage of positive results, whereas with intravenous or corneal inoculations in the same animals the percentage is considerably less. Indeed, in Nichols's³ experience intravenous inoculations in rabbits frequently failed to produce lesions other than of the scrotum or testicle. Moreover, it has been demonstrated by animal experiments that the bone-marrow and the testicle contain the *Treponema pallidum* before the appearance of the chancre.

The susceptibility of the testicle to syphilitic infection is further shown by the work of Warthin,⁴ who frequently was able to demonstrate the *Treponema pallidum* in testicles presenting no gross lesions. Indeed, in cases of congenital syphilis and early acquired syphilis he found treponemata in the testes in which no histological

¹ Being the first of a series of papers on studies of the prenatal transmission of syphilis.

² *Pathologie und Therapie der Syphilis*, Berlin, 1911; Arb. u. d. k. Gesundheitsamte, 1911, vol. xxxii.

³ Bulletin No. 3, War Department Office of the Surgeon-General, Studies of Syphilis, June, 1913, p. 19.

⁴ *Am. Jour. Med. Sc.*, 1916, clii, 508.

changes could be recognized. He has further shown that the testes, next to the heart and aorta, are the most frequently involved organs in syphilitics coming to autopsy. In latent syphilis active lesions will be found in one or the other of these organs if they occur anywhere in the body. The triad of interstitial myocarditis, aortitis and orchitis fibrosa is a pathological complex indicating the occurrence of syphilitic infection in the male. In Weston's⁵ experience an orchitis fibrosa syphilitica chronica is almost a constant finding in paretics coming to autopsy. Symmers⁶ records that among 171 male subjects of late acquired syphilis in the Bellevue Hospital series chronic interstitial orchitis was found 67 times, or 39 per cent.

These circumstances seem to indicate a genitotropic tendency of the *Treponema pallidum*. It is an interesting conjecture to associate this proclivity of the organisms for the generative organs with the possibility that the *Treponema pallidum* has been evolved from a form which was primitively a genital saprophyte.

The testicle of rabbits furnishes an ideal medium for the experimental study of syphilis. This was first established by Parodi⁷ in 1907 and subsequently worked out by Uhlenhuth and Mulzer.⁸ Syphiloma of the testicle in rabbits occurs in three clinical types:

1. The organ swells gradually after an incubation period usually of about three weeks, but may be as long as eight weeks or more, and reaches its maximum size, as a rule, in from four to six weeks. At this time spontaneous retrogression may take place. The testicle not only swells but its consistence becomes considerably increased through infiltration of cellular elements due to the presence of the *Treponema pallidum*. The aspirated juice from the swollen testicle contains an enormous number of actively motile organisms.

2. The occurrence of small, hard nodules, sharply demarcated from the surrounding soft tissues.

3. A chancre of the scrotum as first demonstrated by Hoffman, Löbe and Mulzer,⁹ which appears either as an induration in and under the skin that ulcerates and forms a typical chancre, or as an induration of the tunica and subcutaneous tissue which does not extend to the exterior.

Noguchi¹⁰ has shown that morphological and pathogenic variations in the *Treponema pallidum* (thicker, thinner and average types) resulted in different effects in the production of testicular lesions in rabbits.

Supporting this experimental evidence that the testicle is one of the seats of election of the syphilitic virus is our clinical knowledge

⁵ A personal communication.

⁶ Jour. Am. Med. Assn., 1916, lxxi, 1157.

⁷ Centralbl. f. Bakt., orig., 1907, xlv, 428.

⁸ Arb. a. d. k. Gesundheitsamte, 1910, xxxiii, 183; 1910, xxxiv, 222.

⁹ Berl. klin. Wchenschr., 1913, i, 769; Deutsch. med. Wchenschr., 1913, xxxix, 879.

¹⁰ Jour. Exper. Med., 1912, xv, 2.

that every syphilitic is the potential father of a syphilitic child. However, our knowledge is not yet complete as to the role a pathological involvement of the testicle with syphilis plays in the transmission of the disease. Whether such an involvement is essential or whether the disease may be transmitted independent of an actual disease process in the organ is not definitely known. That treponemata may be borne in the sperm from a healthy testicle is indicated by the fact that the *Treponema pallidum* has been demonstrated in the milk¹¹ from the breast of a pregnant woman in which there was no apparent involvement of the breast; the organism has been found in the spinal fluid¹² in cases both with and without clinical evidences of an involvement of the nervous system. Finger and Landsteiner¹³ demonstrated the presence of *Treponema pallidum* in the semen of syphilitics by animal inoculation. In one case there was clinically an orchitis, but in the other case there was no apparent involvement of the testicle.

PATHOLOGY. The pathology of syphilis of the testicle is essentially microscopic. This becomes apparent when one considers on the one hand the frequent and rather characteristic microscopic picture of the testes of syphilitics in which these organs present no macroscopic changes, and on the other hand the fact that, clinically, syphilis of the testicle is comparatively rare. The pathology of syphilis of this organ is essentially the pathology of tertiary syphilis and is that of a chronic fibrosis with or without gummatous formation.

The histological picture is somewhat variable. In the active cases there exists a plasma cell and lymphocytic infiltration between the tubules, a proliferation of the fibroblasts of the stroma, with thickening of the basement membrane and decreased spermatogenesis. Such changes may occur diffusely or locally. In advanced stages of the disease the spermatogenic epithelium of the tubules may be atrophied; spermatogenesis is therefore absent. However, in some instances, as shown in Fig. 1, part of these structures may be well preserved and properly functioning when the testes otherwise show marked pathological changes. The stroma between the tubules in the later stages becomes thickened and hyaline. In still more advanced stages the entire testis becomes fibroid. Warthin has demonstrated the *Treponema pallidum* in the testes of syphilitics only in the active cellular infiltrations. Grossly the involved organ may be moderately enlarged, globular, indurated and smooth. In the later stages of the disease the organ frequently becomes fibroid, and it is then smaller in size and harder in consistency. However, it is important to bear in mind that in the presence of the

¹¹ Uhlenhuth and Mulzer: Berl. klin. Wehnschr., 1913, i, 769; Deutsch. med. Wehnschr., 1913, xxxix, 879.

¹² See the review of these findings in the paper by Klauder, J. V.: Am. Jour. Syph., 1919, iii, 4.

¹³ Arch. f. Dermat. u. Syph., 1906, lxxxi, 147.

above changes the testis may retain its normal size, shape and consistency, but induration is a persistent feature. According to pathological findings the testes of almost every syphilitic may be said to be diseased, although this is demonstrable clinically in only a small percentage of cases. These pathological changes tend to a progressive loss of spermatogenesis which may cause a premature loss of sexual desire and virility.

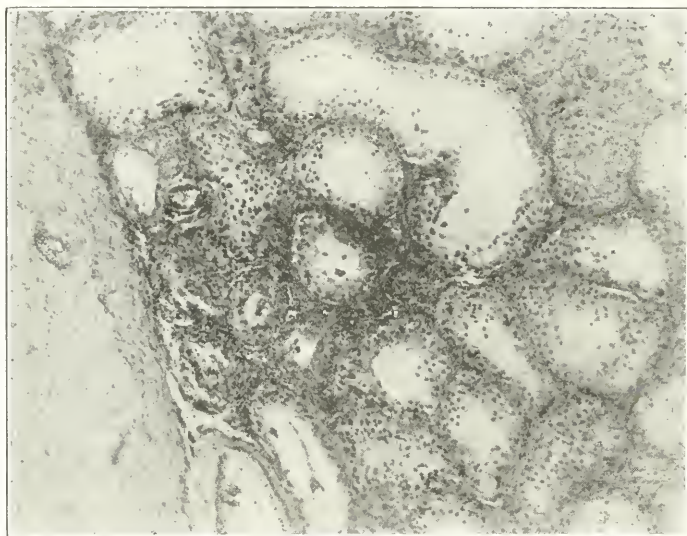


FIG. 1.—Testicle from a parietic. The testicle was clinically and grossly negative. The histological section shows rather extensive areas of fibrosis between tubules with round- and plasma-cell infiltration. The tubules show spermatogenic layers in good state, no atrophy; they were probably functioning. In the area of fibrosis there is present what is probably an obliterated tubule.

Gunmata rarely occur in syphilitic orchitis; the pathology is essentially the pathology of gumma existing elsewhere. They may be single or multiple. Grossly the organ is enlarged and nodular. Adhesions to the scrotal tissue are commonly found. The gunmata often break down and discharge a cheesy matter, in which event secondary infection and subsequent abscess formation is common. The final result is often the formation of a large crateriform ulcer with a sloughing base. Exuberant granulations form and frequently the seminiferous tubules prolapse through the opening with the production of an infected fungating mass of necrotic tissue, constituting a hernia testis. In some instances the breaking down of a gumma is followed by sinus formation.

CLINICAL ASPECTS OF SYPHILIS OF THE TESTES. Syphilitic lesions of the scrotum and of its contents belong for the most part to the tertiary stage of the disease. They are essentially chronic

in type and affect principally the bodies of the testes. The epididymis, together with the constituent structures of the spermatic cord and the layers of the scrotal wall, may, however, become involved either independently or in association with a testicular lesion. The fundamental pathology is the same and results either in a diffuse sclerosis, in the development of gummata or in a combination of these processes. By far the commonest lesion of the body of the testis is sclerotic in type. The most important clinical feature is enlargement of the organ. At first limited to one side the second testis becomes involved later in some cases, although in many instances the second organ escapes.

There is no better description of the syphilitic sclerosis of the testicles possible than that classical one which compares it in physical characteristics to a billiard ball. It is enlarged, rounded, smooth, heavy and insensitive. The normal testicular sensation cannot be elicited even on heavy pressure, notwithstanding which the patient may complain of painful sensations in the afflicted organ. This pain is probably due to traction on the cord or possibly to stretching of normal tissues as the result of the accumulation of fluid in the sac of the tunica vaginalis. Hydrocele of moderate size frequently accompanies syphilis of the testicles.

The epididymis is rarely involved with the billiard-ball type of luetic testicles.

The diagnosis is not difficult if one bears in mind that a diagnosis of essential hydrocele is justifiable only after the condition of the testis, epididymis and spermatic cord are known to be normal. Aspiration of the fluid may be necessary before a satisfactory examination can be made. The syphilitic testicle may be confounded with malignant tumor, especially sarcoma, but the latter grows with greater rapidity, gives rise to considerable pain, as a rule, and remains localized to one side for a considerable period of time. If the external genitals of all syphilitics coming under observation are carefully examined there will be found in a considerable proportion of cases some enlargement and induration of the testes proper. In other instances the epididymii are similarly affected while it is by no means rare to find both structures involved. Oftentimes the condition is possibly not specific in origin, but in a considerable proportion of cases the enlargement and induration, while entirely symptomless, is caused by syphilitic infiltrations, as is proved by the restoration to the normal in size under treatment. Our files contain numbers of illustrative case histories but the following will suffice to demonstrate the condition:

CASE 1.—F. C., aged twenty-six years, single. History of chancre four years ago. Treatment begun in the secondary stage, and consisted of four injections of arsphenamin followed by eighteen months of mercury by mouth.

Present Condition. The patient is entirely without symptoms. He came under our observation because of a 4-plus Wassermann reaction. This test had been suggested by his physician because of the presence of scars on his legs.

Clinical. The evidences of a syphilitic infection are: Scar on the penis. A generalized adenopathy and scars on arms, legs and trunk, having the features characteristic of hues. On account of the rather generalized distribution of these scars they are in all probability the result of a late secondary syphilide.

Local Examination. Both testes are slightly larger than normal, smooth and regular in outline, non-sensitive and indurated. The right epididymis is regular in outline, but is harder and larger than is normal. Both cords are normal to palpation. There is no clinical or laboratory evidence of a Neisserian infection. Serum Wassermann, 4-plus.

The billiard-ball type of syphilitic testicle is not likely to be mistaken for tuberculosis of the testicle, which latter is extremely rare and resembles more the gummatous variety.

Hydrocele may exist only on one side in cases of bilateral syphilitic orchitis; it is rarely large and usually disappears, together with the testicular enlargement, with the institution of antisiphilitic therapy.

The following case history is that of a patient with bilateral syphilitic orchitis of the billiard-ball type associated with hydrocele on the right side. The only subjective symptom in this instance was tumor:

CASE 2.—G., aged twenty-four years; single. History of a penile sore ten years ago. Received local treatment and "blood tonic," self-prescribed.

Present Condition. Swelling of the scrotum of three years' duration. No subjective symptoms except a sense of weight or dragging. No history of trauma.

Clinical. The noteworthy clinical findings are: Scar on the penis at the site of former sore; generalized "bullet-like" adenopathy; a systolic murmur at the base of the heart, transmitted to the neck, with an enlargement of the heart to the left (most likely a luetic aortitis).

Local Examination. Bilateral enlargement of the testicles to about the size of small apples. The testes are ovoid in shape and smooth and stone-like in consistence. There is no tenderness to pressure and the normal testicular sensation is absent. There is a right-sided hydrocele of moderate size. The vasa deferentia and epididymii are normal. Serum Wassermann, 4 plus.

After antisiphilitic treatment there was a marked reduction in the size of the testicles, which became almost normal in size, but they remained harder to the touch than normal organs.

An identical case, the complete clinical notes of which were unfortunately lost, is shown in Fig. 2. This patient also had bilateral

sclerosis of the testicles, with hydrocele on the left side, together with involvement of the epididymis. A nodular circinate syphilide is seen involving the skin over the anterior aspect of the upper left thigh. Note the extensive scarring of the glans penis, evidence of a destructive primary lesion, which was undoubtedly an example of mixed infection. The blood Wassermann in this case was positive, 4 plus.



FIG. 2.—Showing bilateral syphilitic sclerosis of the testicle, associated with involvement of the left epididymis and hydrocele. Note the extensive nodular tertiate syphilide of the left thigh and the extensive scarring of the glans penis.

An instance of unilateral (R) testicular syphilis of the billiard-ball type without subjective symptoms and unassociated with hydrocele is the history of:

CASE 3.—G. B., aged twenty-nine years. Married eight years. Wife is living and apparently well. No children. No stillbirths or miscarriages. Gonorrhoea four years ago. Denies syphilitic infection. Has had no antisyphilitic treatment.

Present Condition. Swelling of the scrotum of one year's duration. No other subjective symptoms. No history of injury.

Clinical. The noteworthy clinical findings are: General adenopathy and a nodular circinate syphilide on the shaft of the penis. The pupils are equal but sluggish in reaction to light.

Local Examination. The right testicle is enlarged to about the size of a hen's egg (Fig. 3). It is ovoid in shape, quite indurated,

but with a smooth surface. Both tenderness and the normal testicular sensation are absent. No fluid present. The epididymis and cord are normal on palpation. The left testicle is normal. Serum Wassermann, 4 plus.

After antisyphilitic treatment there occurred a reduction in the size of the testicles. The patient was not observed sufficiently long for an expression as to the final outcome.



FIG. 3.—Illustrating history of Case 3.

The following account describes a case very similar to the foregoing, except that the testicle was very slightly enlarged. It will be observed in reading these case histories that in the majority of instances the patients presented other evidences of lues. It will also be observed that when mention is made of the results of treatment the testicle is described as having been reduced in size but as remaining indurated. To this one might add that with prolonged treatment and the consequent absorption of the cellular infiltration the testicle is likely to become somewhat atrophic in size, but retains, as a rule, at least in part, its spermatogenic function.

The following case history is that of a patient with unilateral syphilitic orchitis of the billiard-ball type, with moderate enlargement of the testicle:

CASE 4.—H., aged twenty-six years. History of a genital lesion which is indefinitely given as two years ago. Received only local treatment. Denies gonorrhoea.

Present Condition. The patient was referred to us because of a history of having had a genital lesion. He had no subjective complaints but is conscious of a slight enlargement of the right testicle. This he first noticed one year ago.

Clinical. Extensive scar involving glans penis, which is partly destroyed. Many scars on both legs; these are in nature characteristic of scars resulting from healed late secondary or tertiary syphilides. Generalized adenopathy.

Local Examination. The right testicle is enlarged slightly, it is very hard, but smooth in surface, contour and not tender. There is no fluid present. The epididymis and vas deferens are normal to the touch. Examination of the left scrotal contents is negative. Serum Wassermann, 4 plus.

After antisyphilitic treatment there was a reduction in the size of the right testicle, but it remained quite indurated.

There was recently referred to us in the genito-urinary clinic at the Pennsylvania Hospital, a negro, aged thirty-six years, whose left testicle had been removed eight months previously. The clinical diagnosis was tuberculosis, but the pathological confirmation of this is not obtainable. The patient gave the history of chancre sixteen years previously. On examination the right testicle was found to be uniformly enlarged, smooth, indurated and very tender to the touch. The epididymis, spermatic cord, prostate and seminal vesicles were normal. The urine was chemically and microscopically normal. Serum Wassermann, strongly positive.

After the first injection of arsphenamin the testicle became somewhat reduced in size. Since then, with two months' additional treatment, the testicle has reached almost the normal in size.

A somewhat similar case (unilateral (right) syphilitic orchitis, of billiard-ball type, with hydrocele) is the one next to be described. This patient had been operated upon for right-sided hydrocele before he came to the clinic at the Pennsylvania Hospital in March, 1919.

CASE 5.—P., aged fifty-four years. Admitted to the clinic in March, 1919, with the history of a scrotal swelling of some months' duration. Owing to the inability of the patient to speak English a complete history of the case was not obtained. It seems, however, that he had previously been operated upon for hydrocele.

Clinical. The only general evidence of a syphilitic infection is a generalized adenopathy, otherwise physical examination is negative.

Local Examination. The skin of the scrotum shows an operative scar. There is a right-sided scrotal tumor present, which is the size of a small orange. This mass is firm in consistency, dull on percussion and rather irregular in outline. There is a nodular mass in the region of the epididymis, which is probably due to operation for hydrocele. Tenderness is absent. Examination of the left scrotal contents is negative. Serum Wassermann, 4 plus.

After the institution of antisyphilitic treatment the mass immediately became reduced in size and at the present writing the right scrotal contents are normal to palpation, except for the irregularities in the location of the epididymis.

The noteworthy feature in the following case of painful unilateral syphilitic orchitis of the billiard-ball type is the unusually large size of the tumor which gave rise to considerable dragging pain.

CASE 6.—F. C., aged forty-eight years. Twice married, the first time eighteen years ago. First wife had three miscarriages and two children, who are living and alleged to be healthy. The second wife had three miscarriages which were self-induced. The patient admits a urethral discharge ten years ago. Denies syphilis. No history of trauma.

Present Condition. Six months ago he first noticed a swelling in the right side of the scrotum. This soon became associated with inguinal pains and a dragging pain in the scrotum when walking.

Clinical. No stigmata of syphilis. General physical examination is negative.

Local Examination. The right testicle is about the size of an orange. It is ovoid in shape, smooth, indurated and tender to the touch. The right epididymis is normal, as is also the cord. There is a small hydrocele present. The left scrotal contents are normal. Serum Wassermann, 4 plus.

Following the administration of arsphenamin, mercury and potassium iodide the pain and tenderness disappeared and there was a marked reduction in the size of the testicle.

Thus far we have not mentioned the terminal living pathology of luetic orchitis except to say that atrophy sometimes follows. This may occur when no treatment is given and the disease then becomes locally quiescent. Rarely does the skin become adherent and ulcerated. The tunica vaginalis usually becomes thickened in one or more places, with the primary formation of hydrocele, which later may become absorbed, whereupon the sac suffers adhesive obliteration.

The atrophic testicle following luetic infection is an irregular, indurated structure in contrast to the small, soft and smooth organ resulting from mumps.

The comparatively rare gummatous form of syphilitic orchitis unlike the sclerotic form shows a marked tendency to form adhesions with the skin and eventually to lead to the formation of deep crateriform ulcerations through which the necrotic testicular tissues may herniate.

These terminal stages in the development of gummatous orchitis were commonly seen a decade ago and especially in the wards of the large municipal hospitals, but they are now extremely rare.

Gummata of the testicle may coexist with diffuse syphilitic orchitis or one or more gummata may be found in an otherwise

healthy testicle, although this is very rarely met with. They vary in size from a pea to a walnut. The tunica is subject to the same changes as in the diffuse form of the disease.

In the case about to be described the testicle was removed on the mistaken diagnosis of tuberculosis. In this, which is a case of hereditary syphilis, the treponema was found.

The following is the case history of a patient with hereditary syphilitic orchitis of gummatous type; orchidectomy; demonstration of the *Treponema pallidum* in the tissues.

CASE 7.—H. McL., aged twenty-one years; single. Denies venereal disease; indeed, the patient denies having been exposed to venereal infection. Father and mother were killed in a railroad accident. They were in good health prior to the accident. One sister is living and in good health. Family history is otherwise negative. The patient had always enjoyed good health until the onset of the present trouble.

Present Condition. Painful swelling of the right testicle. About one month ago he fell, injuring the organ, since which there has been considerable pain and swelling. For the past two years the right scrotum has been slightly enlarged but not painful.

Clinical. Ill-developed individual of underweight. Forehead is prominent, but otherwise there are no stigmata of syphilis. General physical examination negative.

Local Examination. The right testicle is enlarged, nodular, indurated and tender. The epididymis and vas deferens are normal to the touch. The prostate and seminal vesicles are negative to palpation.

The patient was operated upon, with removal of the right testicle. Grossly the testicle was moderately and irregularly enlarged and firm in consistency. Small nodes were scattered throughout the organ. This appearance suggested gummata to the pathologist, who then examined the secretion from the section surface of the mass and was able to demonstrate treponemata (India-ink method). The histological examination disclosed a picture characteristic of gumma. The Wassermann reaction was subsequently reported as positive, 4 plus.

The clinical differentiation between tuberculosis and syphilis of the testicle should not be difficult. Primary tuberculosis of the body of the testis unassociated with tuberculous epididymitis is an exceedingly rare pathological lesion. No operation should be performed in any case of testicular tumor of doubtful nature until a Wassermann test of the blood is made; and no operation should be performed in a case of this kind when the clinical diagnosis is uncertain, regardless of the result of the Wassermann test, until the therapeutic test is applied.

The foregoing case histories illustrate the commoner varieties of syphilitic lesions of the scrotal contents. We will now describe an

extraordinary case of syphilitic epididymo-orchitis associated with chronic or subacute diffuse inflammatory cellulitis of the scrotal walls:

CASE 8.—J. H., aged fifty-eight years; single. History of gonorrhoea forty years ago. Denies syphilis. No history of traumatic injury to the scrotum.

Present Condition. Patient complains of a painful swelling of the scrotum. Six months ago there was a slight swelling of the scrotum, which for a time grew slowly and painlessly. About two weeks before the patient consulted a physician the mass grew rapidly and became painful. Soon the evidences of inflammation appeared and the patient consulted a surgeon, who advised operation. Multiple incisions were made in the scrotal wall and a large, irregular mass was discovered, filling the right half of the scrotum. The wall of the scrotum was leathery in consistency and the underlying mass tough and of irregular outline. The diagnosis of gumma was suggested at the time of operation. No pus was found and the operation was terminated. Subsequently a serum Wassermann proved to be strongly positive. The patient came to our notice with a chronic lymphedema of the scrotal wall and an irregular, indurated, ill-defined mass in the right scrotal sac. Following the administration of arsphenamin, mercury and iodide of potassium the subjective symptoms rapidly disappeared and the lymphedema of the scrotal wall, together with the underlying tumor underwent almost complete resolution. The left testicle had apparently escaped involvement in the disease process.

Cellulitis of the scrotal skin rarely accompanies syphilitic orchitis, so that the case just described is in some respects unique. Cases of syphilis have been reported, however, in which the scrotum became enlarged in the absence of disease of the scrotal contents. These are usually described as instances of syphilitic lymphedema or elephantiasis.

Levy-Bing and Gerbay have described a case of elephantiasis of the scrotum which was undoubtedly a lymphedema of the scrotal wall secondary to two erosive chancres situated near the base of the scrotum.

We have at the present time a case of pseudo-elephantiasis of the penis and scrotum under treatment in the genito-urinary clinic of the Pennsylvania Hospital; the lymphedema of the scrotum is due in this instance to lymphatic obstruction caused by inguinal adenitis of specific origin. The scrotum is enlarged to more than five times its normal dimensions.

Levy-Bing and Gerbay describe an edema of the scrotum to which they apply the term "éléphantiasis syphilitique primitif." This condition, they say, has been described only once before in a case reported by Meneco Villapadierno.¹⁴ The affection they describe

¹⁴ M. Annales des Maladies Vénériennes, November, 1917.

began as an edema of the scrotum on September 25, 1917. This increased rapidly in size, and four days later the scrotum was increased 17 cm. in the long diameter. The condition promptly subsided with treatment. These cases are, so far as we know, unique clinical types of syphilis of the scrotum.

Epididymitis of syphilitic origin is extremely rare, but, as the few writers who have recently contributed to this subject have shown, the condition frequently exists but goes undiscovered.

In the recent contributions to this subject by Lisser and Hinman,¹⁵ Klauder¹⁶ and by Michelson,¹⁷ special attention is directed to this fact and a more thorough physical examination of the external genitals of syphilitics is urged.

Of the several clinical forms of the disease the chronic indurative type is by far the commoner. Subacute syphilitic epididymitis, which occurs usually in the secondary stage of the disease, is relatively common, while the gummatous variety, which is a late tertiary lesion, is extremely rare.

Lisser and Hinman call attention to the fact that the majority of cases of syphilitic epididymitis reported in the literature occurred during the secondary stage of the disease. They quote Fournier who found eight cases in which involvement of the epididymis took place within a few months from the time of appearance of the chancre.

These older figures are entirely at variance with our clinical experience in which epididymitis occurring during the secondary stage of the disease is, next to the gummatous, the rarest form of syphilis of the epididymis. In the past, syphilitic epididymitis has been considered an extremely rare condition except as an associated lesion with orchitis. We are entirely in accord with Lisser and Hinman, who regard this prevailing view as a misconception of the true nature of the disease. We cannot agree with them, however, in their acceptance of the ancient view of the frequency of epididymitis during the secondary stage of the disease. In speaking of clinical types which these writers divide into the acute and the chronic, they describe the former as follows: "The pain may be very severe and is increased by movement or disturbance. Walking is almost impossible. The entire epididymis is involved, but especially the head. The surface is smooth and the testicle and epididymis can be accurately distinguished one from the other. After a few days the acute process subsides and there follows a chronic course as above. The testicle is not involved."

This sequence of acute followed by chronic epididymitis of syphilitic origin we have never seen, and the recorded experience

¹⁵ Am. Jour. Syph., 1918, iii, 2.

¹⁶ Urolog. and Cutan. Rev., 1919, No. 8, vol. xxiii.

¹⁷ Jour. Am. Med. Assn., 1919, No. 19, vol. lxxiii.

of most syphilographers does not support their belief. In fact, since the original observations by Droan,¹⁸ of Lyons, in 1863, and Fournier's¹⁹ confirmation in 1875 of Droan's statements, epididymitis occurring during the secondary stage of the infection has been generally considered an evanescent condition, which undergoes complete resolution with the disappearance of the cutaneous lesions. Acute syphilitic epididymitis during the tertiary period of the disease is exceedingly rare, but in this instance is followed by demonstrable chronic inflammation.

Epididymitis occurring in the secondary stage may or may not give rise to subjective symptoms, and in by far the greater number the disease does not run an acute course.

As Fournier and Balme²⁰ originally showed, it is only in exceptional cases that the condition is ushered in by acute pain and tenderness sufficient to confine the patient to bed. The majority of these cases are characterized by an indurated swelling of the head of the epididymis, often bilateral, which is rarely larger than a small bean. It gives rise to no discomfort and the patient is ignorant of its presence as a rule. Occurring in the third or fourth month of the disease it is contemporary with the cutaneous lesions. With the disappearance of the latter the condition of the epididymis is restored to the normal in so far as can be determined by physical examination.

The course of events is quite different with the chronic indurative type of the disease. The underlying cause here is sclerosis, which does not disappear spontaneously. The condition is usually symptomless. It may, however, as in the case reported by Lisser and Hinman,¹⁵ give rise to pain and tenderness. More frequently the epididymal lesion is discovered by accident or during a routine examination.

One or both epididymii are enlarged, indurated and club-shaped, the globus major presenting the most marked enlargement. The enlarged globus major has been called by the French the helmet crest and fits over the upper end of the testis proper in much the same manner as the adrenal body rests on the upper pole of the kidney. The diseased areas are thickened, irregularly indurated and somewhat nodular. The epididymis is easily outlined on palpation and is not adherent to the skin of the scrotum or to the testicles. The testis proper may be normal in size or slightly atrophic, and there may or may not be a moderate-sized hydrocele present.

Congenital syphilitic orchitis is not uncommon, but syphilitic epididymitis of congenital origin is extremely rare. That congenital syphilis does attack the epididymis is proved by the oft-quoted cases of Abbott²¹ and of Comby.²² The patient in the case reported

¹⁸ Arch. gén. de méd., 1863, ii, 513 ff, 724 ff.

¹⁹ Du sarcocele syph., Paris, 1875, p. 4.

²⁰ Epididymites syphilitique, Thèse de Paris, 1876.

²¹ A System of Syphilis, D'Arcy, Power and J. Keogh Murphy, i, 319.

²² Annales de dermatologie, 1889.

by Abbot was an infant, aged nine months, who had a large broken-down gumma in the epididymis. Comby's patient, an infant, aged six weeks, had an active secondary syphilis, together with a large nodulated and indurated epididymis. In the discussion which followed the presentation of this patient at the Clinique des Médecines de l'Hôpital St. Louis, Fournier displayed an extreme interest in the condition, remarking its importance in proving that the epididymis to the exclusion of the testis proper could be the seat of syphilitic lesions of congenital origin. The differentiation from gonorrhœa is simple. The globus minor is never involved in the latter disease, which is more acute, and is often associated with a slight febrile reaction. In the subacute forms of gonorrhœal epididymitis the differentiation is more difficult, but the associated urethritis will aid in the diagnosis, and if doubt still exists the demonstration of an infected prostate and seminal vesicle is of great importance. Syphilitic epididymitis rarely exists to the exclusion of other syphilitic lesions, which should be carefully searched for in doubtful cases. The differentiation from tuberculosis is often a matter of extreme difficulty. In these cases it is doubly important not only to make a thorough search for the other evidences of these diseases but to make repeated examinations of the blood, and in the event of failure of all other diagnostic means to give a diagnostic injection of tuberculin and to prescribe antiluetic treatment. Carcinoma of the epididymis resembles syphilitic epididymitis, but only in its very earliest stages. No operation should be undertaken until all diagnostic means have been exhausted and the therapeutic test thoroughly applied.

SYPHILITIC EPIDIDYMITIS. The concurrence of orchitis and epididymitis is a relatively common manifestation of late syphilis. The disease may begin concomitantly in the two organs, but the more usual course of the disease is that of primary involvement of one organ, usually the testicle, with extension to the other. The sequence of events rarely takes place in the sclerotic form of the disease, which remains localized to the part primarily involved. The natural tendency of the gummatous variety is to involve contiguous parts first by inflammatory inclusion in the disease process and later by ulcerative involvement. In some instances the site of origin of a gummatous epididymo-orchitis cannot be determined, because the testicle and epididymis have become transformed into a single gummatous mass, usually associated with a thickening of the tunica vaginalis and hydrocele. The majority of these cases prove on pathological examination to be primary gummatous orchitis, with secondary inclusion of the epididymis. The natural tendency of this form of the disease is to cause destruction of the underlying skin, with the production of the familiar crateriform ulcer. Hernia testis is a common sequel of the ulcer stage.

The gummatous variety of epididymo-orchitis is frequently mistaken for tuberculosis or malignancy. Gummatous epididymitis

in the absence of testicular involvement begins as one or more rounded nodules which are usually situated in the globus major although primary involvement of the globus minor has been reported. The clinical course of the disease is similar to that of gumma of the testicle with perhaps a greater tendency to sclerosis and subsequent atrophy and a lessened tendency to ulceration with destruction of the underlying skin. It is an extremely rare form of syphilis of the epididymis.

In the subacute form of the disease syphilitic epididymitis is likely to be mistaken either for a low grade Neisserian infection or tuberculosis.

The following instance is the case history of a patient with gumma and tuberculosis of the left epididymis:

CASE 9.—F. D., aged twenty-eight years. Married six years ago. Came to this country from Russia five years ago. Wife is living and well. No history of miscarriages. One child living and well.

Mother and father died of tuberculosis. One brother is living and well. One brother died as the result of an accident. Denies venereal infection.

Present Condition. Painful swelling in the right scrotum. Onset about five months ago. No history of injury, although he attributes the swelling of the "testicle" to heavy lifting. Soon after its appearance the swelling was incised and, according to the patient's statement, pus was evacuated. A persistent sinus remains and he has complained of considerable pain.

Clinical. No general evidence of tuberculosis or of syphilis.

Local Condition. The globus major of the left epididymis is about the size of a walnut and quite tender to the touch. Three sinuses are present which open on the anterior surface of the scrotum. Palpation of the remaining portion of the epididymis, testicle and cord is negative. The contents of the right scrotum are normal.

A smear made from discharge from the sinuses was said by the pathologist to contain the tubercle bacillus. Serum Wassermann, negative.

The diagnosis of tuberculous epididymitis was made and the epididymis was removed. The epididymis was found to be grossly normal except the globus major which contained a tumor about the size of a walnut. The tumor was hard and cut with increased resistance. These findings led to an examination for the *Treponema pallidum* which were demonstrated in the surface scrapings by means of the India-ink method.

Subsequently three Wassermann tests were negative (both alcoholic and cholesterolized antigens used). A provocative Wassermann was likewise negative. Stained sections were submitted to Dr. Paul G. Weston for examination. His report is as follows:

Stain, Levaditti. No treponemata found in any of the sections

examined. Stain, fuchsin for tubercle bacilli. No bacilli found. Stain, hematoxylin-eosin. Very prominent are a number of small necrotic areas occurring close together. The central portions are surrounded by outer zones of fibroblasts, small lymphocytes and a few plasma cells. Several giant cells are present at the outer edge of the necrotic centers. These centers contain numerous, blue-staining irregular tissue fragments, but there are no recognizable remains of bloodvessels or connective tissue present. Surrounding the zones of fibroblasts and round cells are areas of dense fibrous tissues which show no hyaline change. The only bloodvessels seen are a few newly formed capillaries in the zone immediately surrounding the necrotic areas.

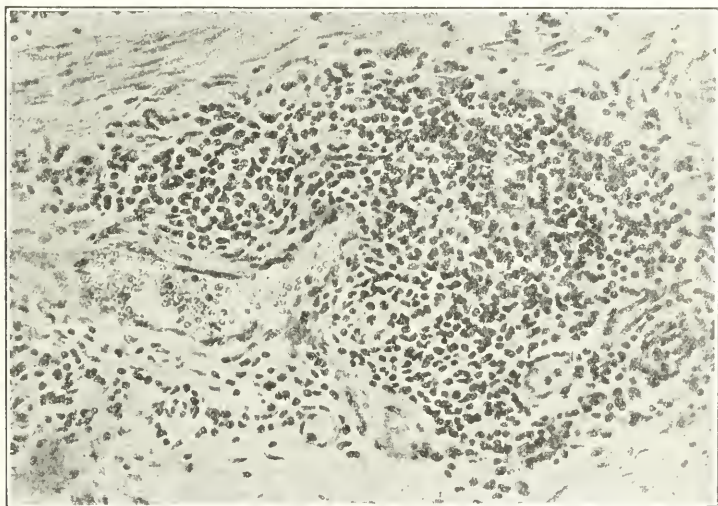


FIG. 4.—Photomicrograph of section of the epididymis, showing round- and plasma-cell infiltration adjacent to capillary.

The interstitial tissue of the epididymis is here and there infiltrated with round and plasma cells. The small vessels show a distinct perivascular infiltration, with plasma and round cells (Fig. 4), the former in large numbers. The vessel walls are normal.

Histological Diagnosis. Syphilis of the epididymis, tubercle, possibly gumma of the epididymis.

Clinically this case seems to be one of tuberculosis. The diagnosis is further supported by the finding of organisms which were looked upon as tubercle bacilli. If we accept as correct the recognition on the part of the pathologist of both the treponema and tubercle bacillus in the specimen, there can be no question of the duality of the infection. The case is of greatest interest to us because, from the pathological studies of the tissue sections, the diagnosis of syphilis seems certain, and yet the patient was historically and otherwise negative for venereal infection. Further-

more, the blood Wassermann test was persistently negative. There is, of course, a great possibility of error.

In the recognition of tubercle bacilli in lesions of the external genitalia and especially in pus from a sinus of the scrotum, there is likewise some uncertainty attached to the recognition of treponemata in India-ink stained specimens. We believe, however, that this is an instance of dual infection of the epididymis because of the clinical features so suggestive of tuberculosis and the microscopic demonstration of syphilitic areas in parts of the epididymis remote from the necrotic areas.

We wish to acknowledge our thanks to Dr. Paul G. Weston, pathologist at the Warren State Hospital, Warren, Pa., for examining pathological specimens and for supplying us with pathological material for study.

THE TUBERCULOSIS PROBLEM AND THE GENERAL HOSPITAL.

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AND

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ONLY a little over a decade ago the present-day, well-nigh universal interest in the antituberculosis movement had its inception. During this period, progress has been made and results have been achieved which are beneficial both to the people at large and to the unfortunate tuberculous. Many millions of dollars have been appropriated and spent in the erection of new and in the enlargement of existing sanatoria (whether altogether wisely or not is still a moot question). With the expansion of such facilities there developed simultaneously greater interest and improvement in the methods of diagnosis of early pulmonary tuberculosis. The general practitioner was aroused to the great importance of the early recognition of this serious malady. He was encouraged not only to make his diagnosis early but to submit it promptly to the patient or his family. A frank and open mind in this matter supervened upon the existing one of doubt and hesitation. The patient in turn learned that the diagnosis of pulmonary tuberculosis did not necessarily seal his doom and the new mental attitude of hope and optimism, frequently reiterated, assisted many unfortunates in regaining their health with the resulting happy consequences of restoring to their dependents, their earning capacity as bread-winners, and to themselves as heads of families that sturdy spirit of independence and self-respect universally admired in the citizenry of a free and enlightened commonwealth.

The educational phase of the campaign among the laity, the organization method employed in the subdivision of large cities into coöperative districts, each with its own clinic, the prophylactic work among the other members of the patient's family, particularly the children, have all played their relatively important role in securing those happy results which we may now contemplate with pardonable pride and satisfaction.

While definite progress in the antituberculosis crusade has undeniably been recorded, on close analysis it is evident that one phase of our plan of campaign is open to serious objection.

To understand more clearly what is meant, it is necessary to analyze the various factors that now enter into the strictly medical plan of our work.

That relatively small class of tuberculous patients, who are fortunate in possessing sufficient means to finance themselves all through their illness, for obvious reasons, are excluded from consideration in the study of this matter.

The first agency that the tuberculous patient who seeks assistance comes in contact with is the tuberculosis dispensary. In all the large centers of population, dispensaries have been erected in which it was hoped the correct diagnosis of the presence or absence of pulmonary tuberculosis could be determined; the negative cases to be discharged and for the positively diagnosed cases, the proper choice of treatment depending upon the stage of illness and degree of activity could be selected.

THE DISPENSARY. The dispensary is indispensable. It has rendered faithful service in the past and is now daily performing a very important function. That it has not been as efficient as had been hoped is both regrettable and excusable. But the fault lies not so much with the dispensary as with those responsible for its creation, in that too big a task was laid out for it from the very outset. The limitations of the dispensary are many and should be appreciated.

While its facilities are sufficient for the majority of cases, they are insufficient for those cases in which accurate and time-taking study is necessary. To enable any resident of a large municipality to secure the diagnosis of the existence or absence of pulmonary tuberculosis is its duty to its citizens. Necessarily such dispensary must always be the seat of intense activity. Its methods naturally are hurried. The remedy lies therefore in supplementing the dispensary activities with hospital facilities for that group of cases for which the dispensary has proved itself inadequate.

The deficiencies of the dispensary are reflected in the complaints of the sanatorium, from which, as variously estimated, from 5 to 20 per cent. of all admissions are discharged as non-tuberculous.

It is clear that this is not the fault of the sanatorium nor yet of the dispensary. The weak link in the chain lies in the absence or in the inadequacy of hospital or ward facilities to coöperate with the

work of the dispensary. While sanatorium facilities grew apace there has been no growth in the ward facilities of our large hospitals. The dispensary has been provided—the sanatorium, too—but the hospital ward has been neglected. It should have been foreseen that to ensure the best results in the sanatorium, proper correlation is essential between it and the dispensary via the hospital ward.

Not only has the dispensary displayed its limitations in the matter of diagnosis, but also in the matter of proper selection of cases for treatment, depending upon their degree of activity. For example a patient presents himself at the dispensary with a small pulmonary lesion which would make him a suitable candidate for admission to a sanatorium, but upon closer study a complication is revealed, such as tuberculosis of the bowel, kidney or bladder, etc., which invalidates this decision and necessitates his admission to a tuberculosis hospital instead. In other words a patient may have an incipient pulmonary lesion and in other respects may be so riddled with tuberculosis as to preclude his admission to the sanatorium. For a proper study of such cases, hospital facilities in conjunction with the dispensary are indispensable and should be provided where they are now absent.

DUTIES AND FUNCTIONS OF THE HOSPITAL TUBERCULOSIS WARD. That the tuberculosis ward is essential in a teaching or university hospital will not be disputed. Since tuberculosis is the most common of all diseases and protean in its manifestations, it is a safe assumption that the young doctor soon after graduation will be called upon to diagnose and treat this disease. He should be trained as thoroughly as possible in the early recognition of its signs and symptoms and its importance should be thoroughly impressed upon his mind. Who knows tuberculosis well, knows something of medicine.

In non-teaching hospitals, where a tuberculosis dispensary is already established, the tuberculosis ward is essential for reasons referred to above. Its facilities may be utilized not only for the study of diagnosis and allocation of patients, but also for the investigation and application of special methods of treatment, such as artificial pneumothorax, etc.

Theoretically, the aim and scope of the modern general hospital are to serve all the sick poor of the community free from prejudice or discrimination. That hospitals in general do not all display this idealistic attitude toward the tuberculous would seem apparent. Some are suffering from phthisiophobia themselves, which can be justified neither by medical science nor human understanding; others are purely dogmatic in their prejudice. It has yet to be proved that danger lurks to the healthy attendants in the tuberculosis sanatorium. By analogy this principle should apply to the tuberculosis ward of the general hospital. If the modern teachings of tuberculosis pathology be true our plea should be unnecessary. We have been shouting from the house tops to the populace that a clean consumptive is no menace to the well, but we have failed to

embody this teaching in the conduct of the general hospital where the tuberculous patient is still gazed at through glasses of "red" with fear and repugnance. Fortunately this has not been the attitude of all general hospitals, and there are notable exceptions. It must be evident that phthisiophobia cannot be eradicated from the minds of the people without engaging the active help and loyal support of the entire medical profession. Hospital authorities could allay this fear to a large extent by the creation of special services, however small, for tuberculous patients.

It seems curious that prejudice should exist against the tubercle bacillus, whereas none exists against other germs, such as the typhoid bacillus, etc. The typhoid bacillus is now everywhere received with open arms by general hospitals, although it has been proved guilty of more infection and death among hospital patients and attendants than ever could be proved against the tubercle bacillus in its palmy days when prejudice against it ran at its height.

In addition to its supplemental work to the tuberculosis clinic the tuberculosis ward should receive the tuberculous patients from the other wards of the hospital. Obviously, the number of such cases would in a measure, be in inverse proportion to the efficiency of the admitting department of the hospital. Tuberculous cases, with few exceptions, should not be admitted directly to the hospital ward. Such should be sent to the tuberculosis dispensary to be admitted or not, according to its own discretion.

The emergency cases, such as acute pulmonary hemorrhage of tubercular origin, should be admitted to the tuberculosis ward for humanitarian reasons if for none other. It should be remembered that occasionally in these cases artificial collapse of the affected lung may prove life-saving.

The plea is here made for the reception of acute surgical conditions in the tuberculous, requiring immediate surgical intervention, *e. g.*, acute appendicitis, incarcerated hernia, etc. Such cases now frequently find the door of the general hospital shut tightly against them. This, in the light of present-day knowledge, is unjust and imprudent. Some provision should be made either on the surgical side of the hospital or in the tuberculosis ward for their reception. Fortunately these cases are few in number; yet they do occur, and they require more than ordinary skill in anesthesia, surgical technic and postoperative care in their treatment. They require the best treatment that the best hospital could offer. The tuberculosis hospital service working in conjunction with its department in the dispensary should be divided into two parts. The one for proved tuberculous patients the other for suspects. There is a group of suspects in whom the diagnosis offers great difficulty. They require careful study in regard to subjective symptomology and also in regard to objective findings, such as variations in temperature, pulse-rate, etc. These patients are manifestly legitimate cases for hospital

study, and when admitted should not be directed to the tuberculosis ward for fear of stigmatizing these patients unjustly. If sent to the general medical service the bond of connection between the dispensary staff and the patient is broken. The ideal plan would be, therefore, to place these patients in a special "observation ward," where the patient remains in the care of a competent physician until the diagnosis is made. By the use of the term "observation ward" no stigma is attached to the patient and if the patient is discharged as non-tuberculous no harm is done. The number of beds in the tuberculosis ward of a general hospital should be proportionate not to the number of beds in the hospital as a whole but to the size and need of the tuberculosis clinic, for since the overflow to the tuberculosis ward from the other wards will be small (where the admitting department is efficient) it is evident that such beds will be utilized almost exclusively by the tuberculosis dispensary. For such dispensary in which about one hundred cases are under active treatment, about 10 per cent., or ten beds in the hospital ward, would suffice. This number should include the positively diagnosed cases and observation ward.

THE SANATORIUM VIEWPOINT. The efficiency of the sanatorium has been seriously impaired by the admission of non-tuberculous cases (5 to 20 per cent.), and far-advanced cases (30 to 50 per cent.). The former are obliged to forsake their work, frequently break up their homes, have their children committed to asylums and preventoria, only to learn after a short stay at the sanatorium that they never had pulmonary tuberculosis and consequently require no treatment. In the meantime a bed has been occupied which might have been utilized more advantageously by one of the many active tuberculous who float about the city for lack of accommodation. Funds have been injudiciously spent, and frequently an additional sum must be extracted from the public funds to rehabilitate the "tuberculous," who, in truth, never had clinical tuberculosis. Moreover, as a result of his confinement in a sanatorium, the innocent individual is now branded with the stigma of tuberculosis, a serious handicap, indeed, in a civilization which for the past twenty years some agencies have thoroughly saturated with phthisiophobia.

On the other hand the far-advanced tuberculous are not only unsuitable for sanatorium treatment but frequently their condition is materially aggravated when subjected to the strict sanatorium régime. These are hospital cases and should be near their homes and relatives. They should not be permitted to obstruct the service in institutions primarily intended for those in whom an economic recovery seems favorable.

These occurrences can best be obviated by the establishment of a tuberculosis ward in the general hospital to coöperate with its out-patient department in the diagnosis in "suspects" who offer unusual difficulty, in diagnosis or in the differentiation of activity or non-activity; the active cases to be sent to sanatoria or hospitals depend-

ing upon their degree of activity and extent of disease; the inactive cases who are not proper public charges to be kept at their work.

In order to ascertain the view of the most competent workers in this field a questionnaire was sent out to many of the largest hospitals and sanatoria in this country. The questions and answers thereto appear in the following tables (1 and 2):

1. Have you a pulmonary service or ward?
2. If so, is it a special service or a part of the general medical service?
3. What percentage of the total number of beds is devoted to pulmonary tuberculosis?
4. Is this growing stationary or receding?
5. If you have no pulmonary tuberculosis service, did you have one, and was it abandoned?
6. If so, why?
7. If your institution never had a pulmonary tuberculosis service, does it consider it desirable, or is it contemplating establishing one.

TABLE I.—TO THE GENERAL HOSPITAL.

	I.	II.	III.	IV.	V.	VI.	VII.
Mass. Gen. Hosp., Boston	Yes	Spec.	%	Sta.	No	..	No
Cleveland City Hosp., Cleve- land	"	"	13	"			
Mt. Sinai Hosp., N. Y. City	"	"	4	"			
Mont. Home and Hosp., N. Y.	"	"	25	"			
Minneapolis City Hosp., Min.	"	"	..				
Med. Chirurgical Hosp., Phila.	"	"	..	Grow.	"		
San Francisco Gen. Hosp., Cal.	"	"	25	"			
Cook County Hosp., Ill.	"	"	..	"			
Dr. A. K. Krause, Baltimore	"	"	..				
University Hosp., Phila.	"	Gen. Med.	..	Sta.	Yes	San. est.	"
University Hosp., Ann Arbor	"	"	12	"			
Met. Life San., Mt. McGregor, N. Y.	"	"	85				
Newark City Hosp., Newark	"	"	..				
Long Island College Hosp., Brooklyn, N. Y.	"	"	2	"	No	..	"
Cin. Gen. Hosp., Cincinnati	"	"	"
French Hosp., San Francisco	"	"	5	Rec.			
Kings Co. Hosp., Brooklyn	"	"	8	"			
Bridgeport Hosp., Bridgeport, Conn.	No	Yes	San. est.	"
Michael Reese Hosp., Chicago	"	No	..	"
Boston City Hosp., Boston	"	"	..	"
Roosevelt Hosp., N. Y. City	"	"	..	"
Peter Bent Brigham Hosp., Boston	"	"	..	"
Johns Hopkins Hosp., Balto.	"	"	..	"
Lankenau Hosp., Phila.	"	"
Post.-Grad. Med. School and Hosp., New York City	"	"
Worcester City Hosp., Wor- cester, Mass.	"	"
Lake Side Hosp., Cleveland	"	"

1. Should all cases as soon as diagnosed be sent to the sanatorium?
2. Does the sanatorium consider it advisable to have beds set aside in the general hospital for the purpose of study, diagnosis, etc., of cases of pulmonary tuberculosis before sending same to it?
3. Does the sanatorium consider it advisable to have a pulmonary tuberculosis service attached to every general medical service of a large institution?

TABLE II.—FROM THE SANATORIUM POINT OF VIEW.

	I.	II.	III.
	Yes	Yes	Yes
Leech Farm Sanatorium			
Cincinnati Gen. Hosp., Cincinnati, O.			
Cleveland City Hosp., Cleveland, O.	"	"	"
Dr. J. Kramer, Montefiore Home Country San.	"	"	"
Michigan State San. for Tuberculosis, Howell, Mich.	"	"	"
North Carolina San., Sanatorium, N. C.	"	"	"
State Tuberculosis San., Hartford, Conn.	"	"	"
Wisconsin State San., Statesan, Wis.	"	"	"
Rhode Island State San., Wallum, R. I.	"	"	"
State Tuberculosis San., Carlsbad, Texas	"	"	"
Cincinnati Tuberculosis San., Cincinnati, O.	"	"	"
National Jewish Hosp. for Cons., Denver, Colo.	"	"	"
Pottenger Cottage San., Monrovia, Cal.	"	"	"
White Haven San., White Haven, Pa.	"	"	"
Gabriel San., Gabriel, N. Y.	"	"	"
Monroe Co. Tuber. San., Rochester, N. Y.	"	"	"
Glen Gardner San. for Tuber., Glen Gardner, N. J.	"	"	"
Catawba Sanatorium, Catawba, Va.	"	"	"
Shelton State Tuberculosis San., Shelton, Conn.	"	"	"
Nopeming San., Nopeming, Minn.	"	"	"
Mount Alto State Tuber. San., Mount Alto, Pa.	"	"	"
Modern Woodmen of American San., Woodmen, Colo.	"	"	"
Otisville San., Otisville, N. Y.	"	"	"
Workmen's Circle San., Liberty, N. Y.	"	"	"
Minneapolis City Hosp., Minneapolis, Minn.	"	"	"
Michael Reese Hosp., Chicago, Ill.	"	"	"
Newark City Hosp., Newark, N. J.	"	"	"
Cook County Hosp., Oak Forest, Ill.	"	"	"
J. N. Adams Memorial, Perrysburgh, N. Y.	"	"	No
Chicago Winfield San., Winfield, Ill.	"	"	"
Bridgeport Hosp., Bridgeport, Conn.	"	"	"
Pennsylvania State San. for Tuber., Hamburg, Pa.	"	No	"
Chicago Mun. San., Chicago, Ill.	"	"	Yes
Rutland State San., Rutland, Mass.	"	"	"
Met. Life San., Mt. McGregor, N. Y.	No	Yes	"
Muirdale San., Wauwatosa, Wis.	"	"	"
Adirondack Cottage San., Trudeau, N. Y.	"	"	"
Westfield State San., Westfield, Mass.	"	"	"
Dr. J. Kamnitz, Montefiore Home Country San.	"	"	"
Loomis San., Loomis, N. Y.	"	"	"
Gaylord San., Wallingford, Conn.	"	"	"
No. Reading State San., Pa.	"	"	"
Jewish Cons. Relief Society, Edgewater, Colo.	"	"	"
State San. for Tuber., Cresson, Pa.	"	"	"
Ohio State San., Mt. Vernon, O.	"	"	"
State Tuber. San., Alto, Ga.	"	"	"
E. R. Baldwin, Reception Hosp., Saranac Lake, N. Y.	"	"	"
San Francisco Hosp., San Francisco, Cal.	"	No	"
Sea View Hosp., West New Brighton, N. Y.	"	"	No
The Henry Phipps Institute, Phila., Pa.	"	Yes	Yes
Dr. Alfred Meyer, Montefiore Home Country San.	"	"	"

An analysis of the information obtained will reveal:

1. That only about 50 per cent. of the large general hospitals (who replied) have a tuberculosis service.

2. In more than half of those that have a tuberculosis service this is a special one.

3. This service wherever existing is stationary and wherever now absent, none contemplate its establishment.

4. Two reply that this service was abandoned because "tuberculosis sanatoria were established in the State." This policy, it must be evident from what has already been stated, is both fallacious and short-sighted.

5. Ninety per cent. of the most competent observers in the field of tuberculosis consider it helpful and advisable to have beds set aside in the general hospitals for the purpose of study, diagnosis, etc., of cases of pulmonary tuberculosis before they are sent to the sanatoria for treatment.

6. Over 90 per cent. of the best sanatoria in this country consider it advisable and necessary to have a special pulmonary tuberculosis service attached to the general medical service of every large hospital. "For years," writes Dr. C. J. Hatfield, "we have pleaded the desirability and real necessity for general hospitals to include tuberculosis wards and clinics in their routine plans. I am familiar with the objections, but to my mind they by no means equal the manifest advantages."

A tuberculosis service comprising ward and clinic in the general hospital is not only advisable but absolutely necessary.

FIBRINURIA: OCCURRENCE IN A CASE OF CARCINOMA OF THE KIDNEY.¹

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SPONTANEOUS coagulation occurs very exceptionally in the urine without an admixture of blood or chyle. If coagulation of the urine occurs spontaneously, when the urine is allowed to stand, the presence of fibrinogen is always indicated and the resulting coagulum is composed of fibrin.

Fibrinogenuria is responsible for the whey-like coagulation of the urine in cases of chyluria due to infection with the *Filaria sanguinis*

¹ From the Urological Clinic of the Peter Bent Brigham Hospital.

hominis. Other than this occasional but well-recognized occurrence in tropical chyluria, fibrinuria is a very unusual and interesting phenomenon.

There have been so few instances of fibrinuria reported that each investigator has made a rather detailed study of his individual case. Since no noteworthy review of these cases has ever been attempted, each writer has felt that those in the literature were fewer in number than is actually true.

As there are only twenty-five authenticated cases in which fibrin coagula have been found in the urine in the absence of blood or chyle, a detailed study of these should be more instructive than a general *résumé* of the literature. The following abstract of the reported instances is given below in chronological order;

1. Nasse, 1836. An unmarried man, aged fifty years, presented himself complaining of "white particles in the urine," nocturia four to five times and occasional sharp pains in the umbilicus and epigastrium. The urine voided was clear and coagulated spontaneously a short time after standing. The coagulum was identified as fibrin and a tentative diagnosis of "urinary disease" was made, but the patient was lost sight of.

2. Neubauer and Vogel, 1872. A woman, past middle-age, presented the clinical picture of an advanced nephritis, with edema and dyspnea. The urine on repeated occasions coagulated on standing and the coagulum was identified as fibrin.

3. Senator, 1874. During the course of treatment of an acute articular rheumatism, by applying cantharides plasters to several of the joints, a middle-aged woman passed many fibrin coagula in the urine. The urine subsequently coagulated entirely when it was allowed to stand, otherwise the urine showed no evidence of renal abnormality. Removal of the cantharides plasters was followed by recovery and no further coagulation of the urine.

4. Bozzolo, 1877. A male, aged eighteen years, presented himself with edema of the extremities, arthritis, epistaxis, intermittent fever and suprapubic as well as right costovertebral tenderness. The urine passed was clear, but coagulated on standing. The coagulum was identified as fibrin. The diagnosis of pyelitis calculosa was made. Several stones were removed from the right ureter and the coagulation disappeared.

5. Bartels, 1878. A young woman suffering from asthma had been applying cantharides paste to the sternal region. She developed frequency and marked pain on urination, and later passed several gelatinous masses through the urethra. The condition recurred for several days, but was relieved immediately on discontinuance of the cantharides applications. The masses were composed of fibrin coagula.

6. Baumüller, 1880. A pregnant woman, aged thirty-eight years,

complained of pain in the right kidney for several weeks. An attack of hematuria had previously occurred. A complete gelatinous cast of the renal pelvis was passed, with a clear urine. The coagulum was firm, solid and white, and gave definite tests for fibrin.

7. Von Jaksch, 1893. A woman, aged forty-five years, had suffered from renal colic for seven years, but had had no symptoms for three years. She appeared complaining that the urine coagulated upon standing. The urine was clear and coagulated almost entirely after standing in a vessel. The coagulum was composed of fibrin and mucin. The diagnosis of "ureteritis membranacea," due to chronic nephrolithiasis, was made. The patient was reassured and discharged.

8. Von Jaksch, 1893. A woman, aged thirty-nine years, was seen complaining of chills, fever, pain in left abdomen and flank, vomiting and swelling in the left loin. The mass was obviously due to the presence of a left perinephritic abscess. The urine, previously normal, now coagulated on standing, forming large, clear, gelatinous coagula, which were found to be fibrin. The woman was discharged without operation, and six months later was well.

9. Alexander, 1893. A man, aged twenty-two years, complained of a previous attack of hematuria and right lumbar pain. On examination there was pain over the right kidney region, but no other findings of note. White coagulated masses were later discovered in the urine and appeared to be fibrin moulds of the ureter. Operation showed no definite pathology in the right kidney. After recovery from operation the patient had severe pain in the right flank and abdomen, with obstruction to outflow of urine from the right ureter (noted by cystoscope). Later a large coagulum was passed, with complete relief of pain. The clot composed of fibrin was a perfect cast of the renal pelvis and calices. The patient had no further trouble.

10. Klein, 1896. This author followed the case of a woman first seen at the age of fifty-two years to her death four years later. The patient gave the clinical picture of an advancing nephritis, but had peculiar cylindrical coagula in a clear urine. These cylinders were composed of fibrin and appeared to be partial casts of the ureters. The patient continued to pass fibrin coagula, although her urine never coagulated after voiding. At autopsy the diagnosis of "granular nephritis" was made ("renal atrophy with amyloid degeneration of vessels and glomeruli.")

11. Greig, 1896. Boy, aged five years, suffering with tuberculosis of the right knee, contracted scarlet fever while in the hospital and recovered without complication. Operation for drainage of sinus in the right knee-joint was followed in ten days by spontaneous coagulation of the clear urine, voided without pain or urinary symptoms. This persisted for three days and later

disappeared permanently. The coagula were composed of fibrin. A diagnosis of "postoperative congestion of the kidney" was made.

12. Frank, 1900. This observer mentions a case in which cylindrical casts of the renal pelvis were passed frequently in a clear urine. The man apparently was suffering from a bilateral renal infection. He diagnoses a "pyelitis productiva" and gives no further data.

13. Trischitta, 1900. A woman, aged twenty-nine years, complained of neuralgic pain in the right lumbar region, with an occasional sharp pain radiating into the groin. She described opaque bodies passed in a clear urine. Later the urine was seen to coagulate on standing. No diagnosis was made. The coagula were identified as fibrin.

14. Rothschild, 1901. A man, aged fifty-nine years, presented himself complaining of dysuria and the passage of white, gelatinous masses. Previous history of hematuria, three years and three months before respectively. Patient passed long, firm, clear fibrin coagula, which appeared to be casts of the ureter. Three months later the patient, having lost much weight and having a palpable tumor in the left kidney, was operated upon. The tumor of the left kidney described as a giant-celled sarcoma was removed. No further coagula were noted in the urine.

15. Losterfer, 1903. A woman, aged forty-nine years, with a past history of rheumatism and migraine, entered the hospital with edema and ecchymoses of the legs, cyanosis and other signs of severe cardiorenal disease. The ophthalmoscope showed marked albuminuric retinitis. The urine repeatedly contained white gelatinous coagula but no blood. The masses proved to be fibrin. The patient died of uremia and the diagnosis of chronic parenchymatous nephritis was verified at autopsy.

16. Isaak, 1903. A man, aged thirty-four years, complained of passing "white clots" at the end of urination. No hematuria or dysuria. Later the urine was seen to coagulate on standing. On cystoscopy the coagula were seen to come from the left ureter. No diagnosis or treatment is recorded.

17. Quinke, 1904. A woman, aged twenty-three years, had repeated attacks of hematuria. She had a palpable tumor in the left abdomen, with loss of weight and strength. At times when the urine was clear there were cylindrical coagula passed and the urine frequently coagulated upon standing. Operation showed the left kidney to be converted into a hydronephrotic sac. This was removed and the patient died on the sixth day. At autopsy the right kidney was found to be cystic. The coagula were identified as fibrin.

18. Imbert, 1905. A man, aged thirty-seven years, during an attack of influenza, had frequency, dysuria and strangury. At the end of each urination he had slight hematuria. Several days later

the urine was seen to coagulate immediately after voiding. The condition lasted several days and disappeared, with recovery from the influenza. The coagula were repeatedly identified as fibrin.

19. Mosse, 1906. A girl, aged fifteen years, passed coagula repeatedly in the urine. The urine also coagulated while being observed. The ureteral specimens obtained at cystoscopy both coagulated on standing. The patient was jaundiced and anemic and the diagnoses of echinococcus cyst of the liver and chronic parenchymatous nephritis were made. No further report is given.

20. Basile, 1906. A man, aged forty-two years, complained of pain in the abdomen associated with urination. Large, white, gelatinous masses were passed which were identified as fibrin coagula. No further report is given.

21. Imbert, 1908. A man, aged forty-four years, complained of coagulation of the urine after voiding. The coagula were identified as fibrin. He seemed otherwise well and was lost sight of.

22. Imbert, 1908. A man, aged seventy-two years, previously syphilitic, presented himself with the complaint of passing coagula in his urine. At times there had also been hematuria. Repeated observations verified the finding of fibrin coagula. The patient became worse and died later of uremia. During the last two months of life no coagula were formed. The autopsy verified the diagnosis of chronic nephritis.

23. Imbert, 1908. A man, aged thirty-three years, had repeated attacks of renal colic, then passed some "gravel," after which the urine repeatedly coagulated upon standing. The coagula were composed of fibrin. The patient was subsequently well.

24. Bouchard, 1911. This reporter observed a case of "cystitis" which repeatedly passed large fibrin coagula. He made extensive chemical studies on the spontaneous coagulation of the urine in this case and decided that desquamated epithelial cells were necessary to bring about the deposit of fibrin from fibrinogen in the urine. His work is interesting but not convincing. His case was not improved by bladder lavage and was not followed further.

25. Emerson, 1913. A woman, four hours before death from chronic parenchymatous nephritis, passed 5 c.c. of urine that formed a coagulum. This was identified as fibrin.

Baumüller states that Koch, in a personal communication, described the occurrence and identification of fibrinuria in a case later found to have been a carcinoma of the kidney. Israel, in his text-book, describes a case in which a renal tumor had broken into the renal pelvis and formed a cone occluding the lumen. White coagulated casts of the ureter were frequently passed in the urine. This appears to have been another instance of fibrin coagula formed in the urinary tract. Fürbringer describes, in his text-book, the occurrence of spontaneous coagulation of the urine in two typhoid patients, both of whom recovered. A cast of the renal pelvis 13 cm.

long was described in one instance. Suter in discussing malignant tumors of the bladder states that fibrinuria may occur very rarely in association with this disease. He quotes no such cases, nor are any found in the literature. Fenwick also states that "the appearance of fibrin coagula in the urine is the very rarest symptom evoked by vesical growths." Eichorst quotes no specific cases of fibrinuria, but states that it occurs "after cantharides applications, in villous tumors of the bladder and endemically in the Isle de France and in Madagascar." The latter undoubtedly refers to tropical chyluria.

I wish to supplement the above *résumé* by reporting the following case, which has recently been under my care.

Henry L., a Jewish clerk, aged fifty-seven years, entered the Peter Bent Brigham Hospital on September 1, 1919, complaining of backache, dull pain under the right costal margin, loss of weight and "clotting" of the urine. The family history was not important. His habits were good. There was a history of mild, fleeting pain in the left flank for seven years. This was non-radiating and not severe enough to worry the patient. He had been obliged to rise once during the night to urinate for ten years, but there was no frequency of urination during the day. The present illness began in September, 1918, following a mild attack of influenza, which left him with a frequent irritating, non-productive cough. At this time the physician who examined his urine told him that it was peculiar, but did not go into detail about the findings. From this time on the patient began to lose weight and had become continually constipated. He would go for several days without a bowel movement, and a resultant abdominal distention and frequent dull discomfort in the epigastrium would be relieved only by vigorous catharsis. In December, 1918, he began to have slight dyspnea on exertion and more or less general weakness. One month later nocturia increased to three times, but there was no frequency during the day, and no hematuria, dysuria or abnormal urine noted.

In April the patient noted that his urine contained grayish-white particles and was somewhat cloudy. He also noticed that the urine became whey-like when standing in a vessel for a few hours. A few weeks after this observation he passed a moderate amount of bright red blood without pain or other associated symptoms. He immediately consulted a physician who gave him some medicine, and he had no further hematuria at that time.

Early in June the patient began to have a dull, "heavy" pain in the right flank and along the right costal margin anteriorly, but this was not severe and caused him no great concern. In the first week in July he consulted a physician because of a slight cough, and after a superficial examination was advised to save his urine in twenty-four-hour amounts. He then noted that his single specimens of

urine voided into the twenty-four-hour container formed a clear gelatinous layer at times, although there was never a suggestion of blood in the urine. He called the attention of his physician to this who examined the urine and told him he had "too much fat in the urine." Later, at his physician's advice, he underwent a cystoscopic examination and was told that he probably had a stone in the left ureter and that his right-sided pain might be due to the added excretory burden on the right kidney. He continued to lose weight and strength and was unable to work. During this time he was placed upon fat-free diet and noted no further coagulation of the urine. Two weeks before admission the patient had a severe attack of colicky pain, localizing itself in the right groin and over the spine of the pubis on the right. The pain was relieved after three hours, but that night he had an attack of hematuria similar to the one in April. In the morning the urine was clear and he has never noted any hematuria since.

A letter accompanying the patient stated that he had been suffering from chyluria, and that though repeated blood examinations had been made no filarial parasites had been identified. A palpable mass in the right flank was also described.

Admission temperature, pulse and respiration were normal. The blood showed 6400 leukocytes; hemoglobin, 55 per cent.; erythrocytes, 3,500,000. The differential count was normal and no malarial nor filarial parasites nor abnormal red cells were noted. The blood Wassermann was negative.

The urine was acid; specific gravity was 1024; a slight trace of albumin was present and occasional red and white blood cells, but no casts. No fat was noted. Phenolsulphonephthalein test showed an excretion of 40 per cent. in two hours.

Physical examination showed marked loss of weight and sallow complexion, but no icterus. The heart and lungs were normal. A mass, smooth in outline, firm and moving on respiration, was felt extending two finger-breadths below the right costal margin. No tumor mass could be felt in the right flank, but there was slight costovertebral tenderness on deep palpation. The genitalia were normal. There was no varicocele present and rectal examination showed normal findings. The mass palpated was obviously the liver, although there was no increase in the area of liver dullness above the costal margin. The impression obtained at this time led to the examination of the feces and complete roentgen-ray studies of the gastro-intestinal tract. These findings were normal in every respect.

Cystoscopy revealed a normal bladder, but on prolonged observation of the right ureteral orifice a small quantity of old blood-clot was seen to come from the ureteral opening. Other than this there was no normal orificial contraction and no efflux noted. The left ureteral orifice was normal, with clear urinary efflux. A No. 6

French catheter passed 30 cm. into the left ureter, but a No. 5 French catheter was only with difficulty passed 10 cm. into the right ureter. The urine obtained from the left ureter was normal in all respects. There was no flow obtained from the right ureteral catheter. The phenolsulphonephthalein appeared from the left kidney five minutes after intravenous injection, and there was an excretion of 25 per cent. of the dye in fifteen minutes.

Left pyelo-ureterogram was normal after gravity injection of 20 per cent. sodium bromide solution. No gravity flow of the opaque fluid was obtained on the right, so 20 c.c. was injected under moderate pressure. The ureterogram showed a tortuous ureter in its lower third, but none of the fluid reached the renal pelvis.

Following cystoscopy it was noted that the bladder specimen of urine, withdrawn at the time of examination, had partially coagulated in the glass. The coagulum made up half of the volume of the specimen and was a clear, grayish-white, transparent, gelatinous mass. The coagulum and urine were carefully studied to determine the nature of this substance. There was no chyle or fat present, no albumose or Bence-Jones protein and no mucin. The jelly gave the characteristic tests for fibrin. These are, in brief: Insoluble in water; stiffening of the coagulum on boiling; insoluble in alcohol; insoluble in neutral solutions; increase in swelling of coagulum on addition of weak acids or alkalies; gradual dissolution in concentrated mineral acid and subsequent reaction as acid albumin. An occasional leukocyte and erythrocyte were found in the centrifuged specimen.

Urine examination on the three following days showed the presence of fibrin masses and shreds in the urine, but no further spontaneous coagulation of the urine occurred after voiding.

Physical examination now made apparent an indefinite palpable mass in the right flank overshadowed anteriorly by the position of the liver. A diagnosis of neoplasm of the right kidney was made.

Operation was performed on September 11 under nitrous oxide and oxygen anesthesia. A right lumbar incision was made and a large nodular kidney was identified. The renal artery and vein were normal and the mass was not markedly adherent to the surrounding structures. The tumor mass was removed with some difficulty because of its size, the perirenal fat being removed without incision. The peritoneum was opened posteriorly and the liver found to be normal in size, consistency and position. The wound was closed without drainage and the patient made an uneventful recovery, being up and about in a wheel chair on the tenth day.

The urine on repeated examinations after operation was normal. The phthalein excretion before discharge was 35 per cent. in two hours. The patient was discharged on October 11 in good condition, having gained eight pounds since operation.

Pathological Report of Dr. S. B. Wolbach. Gross description: Specimen consists of a right kidney tumor weighing 926 gm. and measuring 12 cm. from pole to pole and 10 cm. from the pelvis outward in the median section. In thickness the measurement is 10 cm., not including a thick layer of perirenal fat, which is very adherent to the surface of the tumor mass. The external surface is smooth, but most of the surface presents rounded, irregular nodules, red in color, with the exception of one that is quite firm upon palpation and white in color. Sectioning through the median line in the mass the surface upon rough inspection presents no normal kidney structure or substance, the whole kidney being apparently

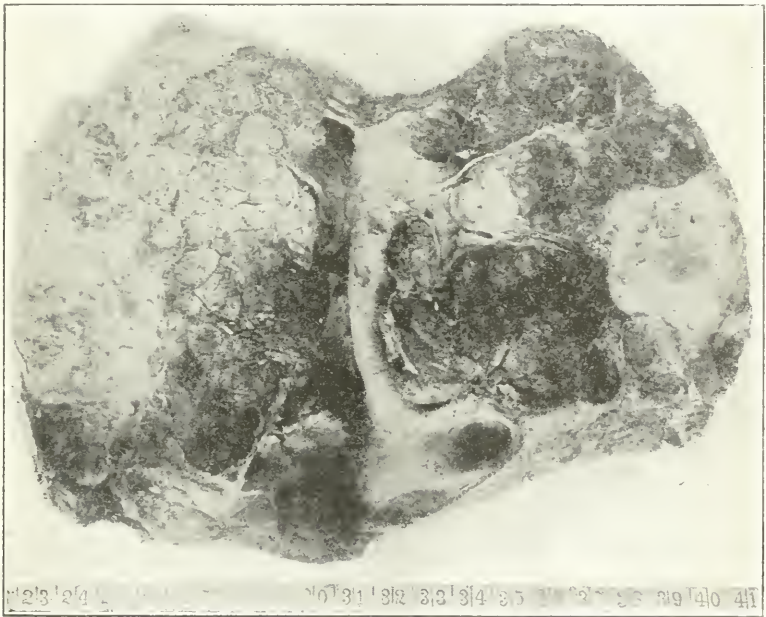


FIG. 1.—Gross specimen of kidney tumor after median section.

replaced by lobules of spongy and firm tumor cells. On close inspection, however, at both lower and upper poles there is still a very thin shell of cortex, measuring not over 2 mm., which shows definite glomeruli. This small amount of renal tissue extends for only 2 or 3 mm. along the edge, when it disappears, becoming a mere layer of fibrous tissue, which surrounds and apparently bounds the growing tumor cells. The pelvis of the kidney is filled with a mass of fat and nodular tissue, which is about 8 cm. long and 2 cm. thick, and in its center there is a small, hard, apparently calcareous mass or nucleus. The entire mass seems to be attached to one side of the pelvis where the lining membrane of the pelvis ends. This membrane is for the most part soft, smooth and glistening,

but there are seen to be small implantation areas of cells. The cut surface of the kidney shows a large, firm, white area about centrally located, measuring 4 x 5 cm. This area stands out in contrast to the rest of the areas of tumor cells because of its white color and firm structure. The other portions of the tumor, which are definitely localized, separated and surrounded by white, fibrous tissue bands, are red in color, of spongy consistency and have a more medullary and glandular appearance. Tissue from the tumor was fixed in Zenker and a frozen section presents the picture of medullary carcinoma.

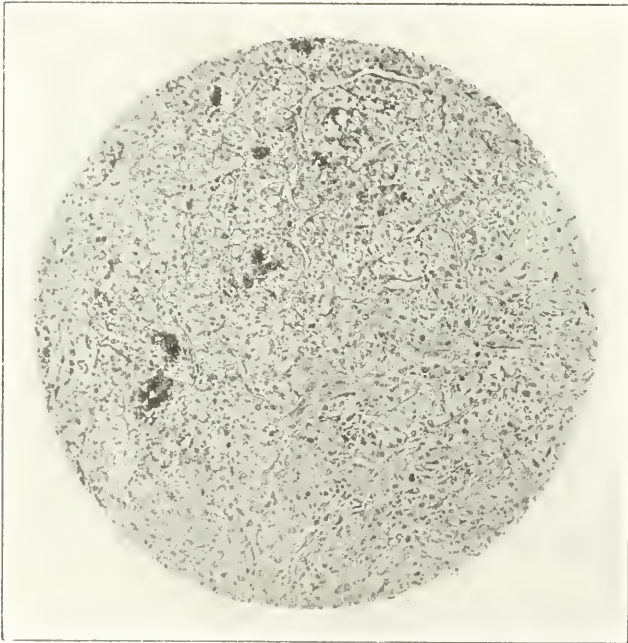


FIG. 2.—Low power ($\times 125$), showing transition from adenomatous to carcinomatous structure.

Microscopic Report: There are sections from four different portions of the tumor stained with eosin methylene blue and with phosphotungstic acid hematoxylin. The sections present widely different appearances according to the portion of the tumor from which they came. Three of the sections present a somewhat adenomatous structure, built up of tubules and small cysts, with papillary ingrowths lined by columnar cells, most of which are of vesicular outline, due to a marked vacuolization. This portion of the tumor is divided up into larger and smaller nodules by a fairly heavy framework of connective-tissue and in some places bands of smooth muscle, the latter possibly derived from the kidney structure. The cells forming tubules are supported by a

very delicate connective tissue abundantly supplied with capillaries, and suggest the renal origin of the tumor (Figs. 2 and 3). Sections stained for fat after fixation in Klotz fixative show a very slight amount of fat, or rather lipid material, as the color of an occasional granule is pale orange. This portion of the tumor contains small areas of hemorrhage, both recent and ancient. The other portion of the tumor corresponding to the dense, white nodule noted in the gross description presents a complex appearance. In one portion it is definitely invading the capsule and has the structure of carcinoma with abundant stroma (Fig. 4). Other portions present solid masses of rather vesicular epithelial cells, with a slight tendency

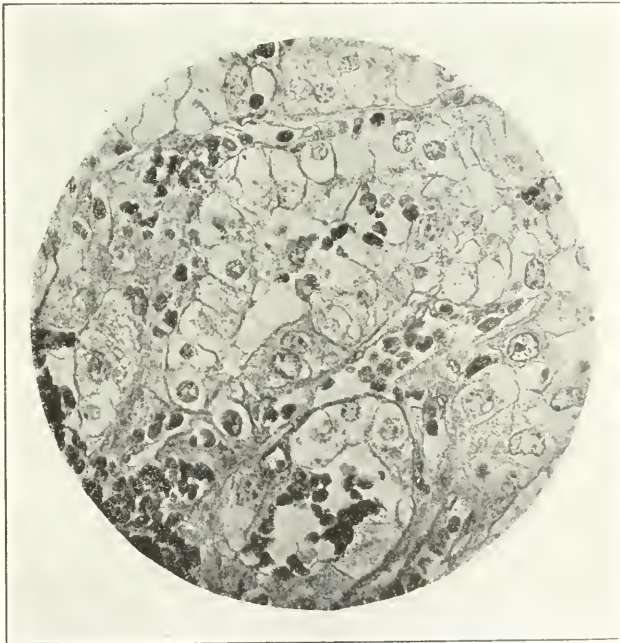


FIG. 3.—High power ($\times 640$) of area shown in Fig. 2.

toward alveolar formation. The bulk of this portion, however, is composed of spindle-shaped cells accompanied by a small amount of diffusely distributed intercellular substance, which stains a feeble yellow with phosphotungstic acid stain, and on the whole presents the appearance of a sarcoma rather than of a carcinoma. There seems, however, to be a transition from the adenocarcinomatous appearance to this architectureless portion (Fig. 5). The cells of both portions have some features in common, namely, in their somewhat vesicular appearance and in the size and chromatin content of the nuclei. It is also worthy of note that these sarcomatous areas contain considerable dark brown, granular pigment

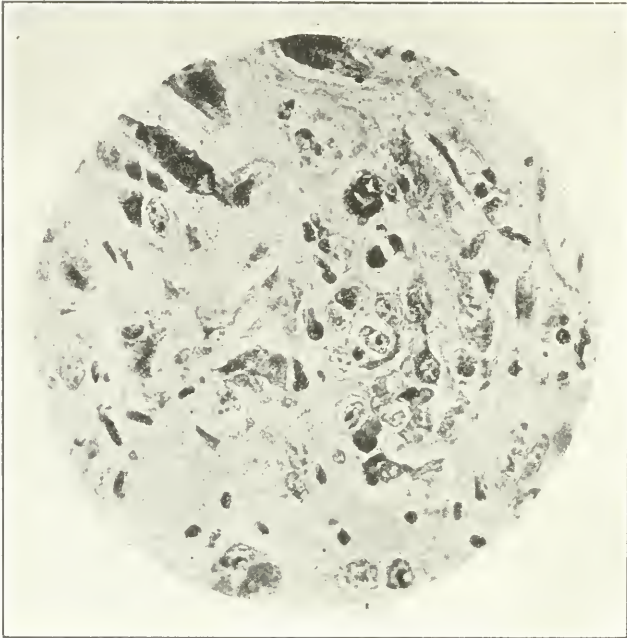


FIG. 4.—High power ($\times 640$) from periphery of tumor showing carcinomatous structure.

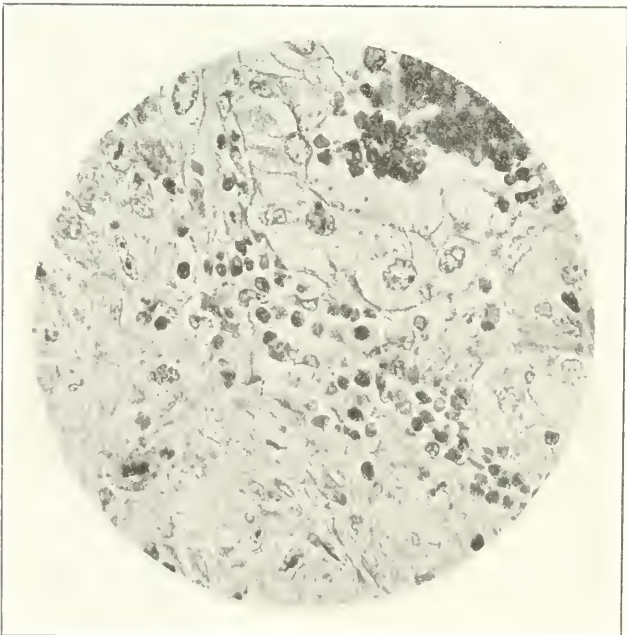


FIG. 5.—High power ($\times 640$), showing proximity of adenoma and sarcoma-like portion. Note mytotic figure in lower right corner.

enclosed within phagocytic cells and my interpretation is that in these sarcoma-like portions we have a simultaneous growth of tumor and fibroblasts which have replaced areas of hemorrhage. Mitotic figures are abundant in all parts of the tumor, particularly abundant in the last described portion.

Comment. Tumor is an adenocarcinoma of renal origin and has in places taken on the characteristics of a more malignant form of carcinoma, with loss of gland-like structure.

Diagnosis. Carcinoma of kidney.

CONCLUSIONS. Spontaneous coagulation of the urine occurs very rarely without an admixture of blood or chyle.

That the fibrin coagula identified in these various types of disease of the urinary tract were chemically and microscopically identical seems evident from the case reports.

That the fibrin found in the urine of the case reported above was not a product of the carcinoma itself, but a result of the associated renal destruction, seems evident from a study of these cases.

The pathological condition underlying the etiology of this condition seems to be a nephritis of varying grade and severity.

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ANTHRAX FROM THE SHAVING-BRUSH AND PRIMARY ANTHRAX MENINGITIS.

By H. W. CAREY, A.B., M.D.,

TROY, N. Y.

SOON after the beginning of the War, numerous cases of anthrax were reported in which the source of the infection was obscure. The first cases were reported in England in 1914 from among the troops in the concentration camps. No history could be obtained of any contact with cattle, hides, meat or wool, nor of any of the known sources of anthrax infection. In nearly every instance the disease made its appearance on the face as a malignant pustule. Later when the United States entered the War anthrax infection made its appearance among our troops in the training camps, although a few scattered cases occurred among civilians.

A typical instance of shaving-brush infection came under the writer's observation and will be introduced at this point in order to include it in a general summary of the subject that is to follow.

M. B., male, aged thirty-four years, a window-washer by occupation, complained of a sore on the right side of the neck, slightly below the angle of the jaw. Four days before, as he was about to shave, he noticed a small pimple on the neck. He had just bought a new shaving-brush for ten cents and was about to use it for the first time. While he was shaving he cut off the top of the pimple and it bled a little. This spot became sore shortly afterward and developed into a pustule, which quickly grew larger, and the neck began to swell. He felt apprehensive and could not sleep well. When first examined the sore measured 2 cm. in diameter. It was indurated and raised somewhat above the level of the surrounding skin. In the center was a black eschar surrounded by vesicles, some 0.5 cm. in diameter, which contained a slightly bloody serum. The skin surrounding this for a distance of 2 or 3 cm. was very red and edematous. The lymphatic glands under the jaw were swollen and indurated. The temperature was 100° and the pulse 96. The

leukocytes were 17,000. A blood culture made the following day developed no growth.

Smears made from the serum in the vesicles contained many long bacilli, with square cut ends. A tendency to chain formation was noticeable. They were Gram-positive. Cultures were made on agar slants and bouillon, and from the latter agar plates were seeded. The colonies on the agar plates and slants developed in twenty-four hours typical medusa-head colonies and in the bouillon the growth formed long threads. The bacilli were non-motile. A small portion of the bouillon culture was introduced into the peritoneum of a guinea-pig. The animal died within twenty-four hours. The necropsy revealed an edema and erythema at the point of inoculation; the peritoneum was edematous and the spleen swollen. Smears and cultures taken from the point of inoculation, the spleen, peritoneal cavity and the heart blood contained bacilli which morphologically and culturally corresponded to anthrax bacillus.

As soon as the diagnosis was established the patient was referred to the surgical service. The affected area was excised completely, with a wide margin of healthy tissue, and the wound sutured without drainage. No local treatment was used and no serum given, as none could be obtained without considerable delay. The temperature and pulse-rate promptly dropped to normal and the wound healed *per primam*. The glandular swelling subsided rather slowly. At the end of one week the patient was discharged well.

An effort was made to cultivate anthrax bacilli from the shaving-brush. The bristles were placed in bouillon tubes and flasks and from these agar plates were seeded. The growth of contaminating organisms was so abundant and spread so rapidly over the plates that no anthrax colonies could be found. While the attempt to find the anthrax bacillus in the shaving-brush was unsuccessful, there can be little doubt that the infection originated from it. The patient's sole occupation was window-washing, and it did not bring him into contact with any of the common sources of anthrax infection, such as cattle, meat, wool or hides. The only possible carrier of anthrax was the shaving-brush, which he used for the first time the day before the sore began.

In the early reports of anthrax cases in England the infection of the shaving-brush was attributed to the "diabolical tactics of the enemy." The investigation made by Coutts¹ offered what appears to be the correct explanation. Before the War began the shaving-brush was made from badger-hair, horse-hair or pig bristles. Soon after War was declared badger-hair could not be used, as it had been imported chiefly from Russia. At the same time there developed a large demand for the shaving-brush by the troops in the training camps. To meet this demand manufacturers used horse-hair and

¹ Anthrax and the Shaving-brush, British Med. Jour., June 30, 1917, p. 882.

pig bristles imported direct from China and Siberia. The former were notoriously dirty and were not properly disinfected. They were responsible for the most of the infections.²

An investigation of the shaving-brush industry was also made in this country, but some time later, in which the infection was traced to both imported hair from China and Siberia and to "local hair" from the Argentine and Chicago. It was found that some manufacturers used the hair just as they received it, on the assumption that it had been disinfected, while others exposed the hair to prolonged boiling or to live steam, both of which seemed to yield satisfactory results. For general use, however, it was recommended that the hair be immersed for several hours in 10 per cent. formalin at a temperature of 110° F.



FIG. 1. -Malignant pustule on right side of neck caused by infected shaving-brush.

The investigation in England recorded 19 cases of anthrax among civilians from June, 1915, to October, 1916, 14 of which were proved to be caused by the shaving-brush and 5 suspected of starting in this way. In the army in France, from 1915 to February, 1917, 23 cases developed, all on the face and presumably from the use of the shaving-brush. No examination of the brushes could be made,

² Anthrax from the Shaving-brush, U. S. Public Health Reports, July 12, 1918.

however, because of the rapid movement of the troops in the field at this time. Among the troops in England there were 18 cases, 12 in the shaving area of the face and 4 almost certainly due to the shaving-brush.

In this country there have been 24 cases of anthrax caused by the infected shaving-brush. Two of these were civilians and the remainder among the troops in the training camps. In 6 of these the anthrax bacillus was cultivated from the brushes and the evidence in the other cases leaves little doubt that they were infected in the same way.

Numerous unsuccessful attempts were made to isolate the anthrax bacillus from the suspected brushes, due chiefly to the fact that cultural methods were used rather than animal inoculations. In the cultural method the enormous number of adventitious organisms on the brushes overgrows the anthrax spores, making it very difficult to identify the anthrax colonies.

Leake and Lederer³ suggest the following method for isolating the anthrax bacillus from the shaving-brush:

One-half of the hair of the suspected shaving-brush is macerated in a mortar with 50 c.c. of normal salt solution. The suspension is pipetted off into large flasks or test-tubes and heated to 80° C. for ten to thirty minutes, in order to destroy the bacteria, leaving only the spores. The fluid is then centrifuged and the sediment used to inoculate mice and guinea-pigs. They advise using 0.5 to 1 c.c. for mice and 2 to 12 c.c. for guinea-pigs. A portion of the sediment may be used for culture purposes. They suggest that the sediment be diluted with salt solution, in order to obtain a good distribution of the colonies when agar plates are used. The colonies that appear suspicious are fished to agar slants and the growth developing on them is used to inoculate guinea-pigs and mice. With this method they were successful in isolating anthrax bacilli in three out of nine new shaving-brushes.

Clinically the cases presented the well-recognized types; the malignant pustule was the most frequent, as might be expected from the mode of transmission. Occasionally instances of septicemia and intestinal and pneumonic infection occurred. There were also 9 instances⁴ of meningeal infection, 3 of which were apparently primary, without any point of entry that could be found. Seven of these were reported from England and two from Canada. They all presented the usual symptoms and signs of meningitis; the onset was sudden and the fatal course of the disease very rapid. The diagnosis in every case was made by finding the anthrax bacilli in the bloody spinal fluid.

³ *Am. Jour. Public Health*, February, 1919, p. 114.

⁴ Roscoe: *Lancet*, March 17, 1917, p. 407. Warren and Williamson: *Jour. Royal Naval Med. Service*, April, 1918, p. 212. Gilmour and Campbell: *Canadian Med. Assn. Jour.*, February, 1918, p. 97.

The possibility of anthrax causing meningitis has received very little recognition in this country, possibly because anthrax has not been a common disease. It has been recognized in Europe, however, since 1874, when Wagner described the pathological changes in two cases that came to autopsy. More recently there has been a number of instances recorded, notably by Merkel, Czyhlarz, Risel, Ziemke, Babes, Fulci and Herzog.

The hemorrhagic character of the meningeal exudate and the blood-stained spinal fluid are emphasized by all these writers, and are characteristic of this type of meningitis. Herzog, after a histological study of the bloodvessels in three cases, explains this as being due to a necrosis in the muscular coats of the vessels which permits the elastica and intima to be protruded by pressure and eventually to rupture. The toxins of the microorganism is believed to be the cause of the necrosis.⁵

SUMMARY. 1. A new method of anthrax transmission from the use of the shaving-brush has been discovered during the War.

2. The hair used in the manufacture of the infected brushes came chiefly from China and Siberia, to a lesser extent from the Argentine and Chicago. The hair was either not disinfected at all or inadequately disinfected.

3. The isolation of the *Bacillus anthracis* from the shaving-brush is accomplished better by the inoculation of susceptible animals than by cultural methods.

4. Meningitis due to anthrax may occur without any apparent point of entry. The spinal fluid is always bloody and contains the anthrax bacilli in large numbers.

⁵ Czyhlarz: *Wien. klin. Wehnschr.*, 1916, xxix, 768. Risel: *Ztschr. f. Hyg. u. Infektionskrankh.*, 1903, xlii, 381. Ziemke: *München. med. Wehnschr.*, 1898, No. 20, p. 765. Babes: *Romania Mediceale*, 10 Jahr., 401. Fulci: *Histolog. u. histopath. Arbeiten über die Grosshirnrinde*, 1913, Bd. vi, Heft 11, p. 1. Herzog: *Beiträge zur path. Anat. u. zur allg. Path.*, ix, 513.

REVIEWS

A TEXT-BOOK UPON THE PATHOGENIC BACTERIA AND PROTOZOA. FOR STUDENTS OF MEDICINE AND PHYSICIANS. BY JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the University of Pennsylvania. Ninth edition, thoroughly revised. Pp. 858; 330 illustrations, a number of them in colors. Philadelphia and London: W. B. Saunders Company.

RECENTLY a new edition—the ninth—of McFarland's *Pathogenic Bacteria and Protozoa* has appeared. One finds many improvements in this over the other deservedly popular editions.

Although composed of fifty additional pages, with more numerous and even better illustrations, the use of finer paper has accomplished a thinner, more easily handled and altogether more attractive volume.

Though revised amid the distractions of army life the author has not been unmindful of the little changes that smooth and clarify. In treating of sciences such as are here dealt with there are many subjects that must be gone into of which our knowledge is far from complete or certain. Happily, for the student at least, when dealing with such subjects, this book does not confuse one with a mass of contending hypotheses and theories, but enables him to leave such subjects with good defensible opinions.

There is again an absence of any systematic arrangement of the subjects presented in Part II. We believe some arrangement, either according to the type of disease produced or according to the organismal cause producing it, would leave the reader with a clearer and more consecutive comprehension of the relation of organisms to disease.

Much has been added to the chapter on suppuration and the gas-forming organisms. The author has incorporated a new chapter on infective jaundice; and in keeping with the increase of our knowledge of the types of the pneumococcus the chapter on this organism has been practically rewritten. Generally the author is conservative in his discussions and recommendations. We are a little surprised to find him recommending unequivocally the therapeutic use of Type II serum in all cases caused by this type of the organism—a mode of procedure that has not met with success or approval at the hands of many workers.

Two very happy features of the book are the descriptions of pathological findings and the presence of charts and the many other efforts the author has made to aid the student in the identification of organisms.

H. F.

WHAT WE KNOW ABOUT CANCER: HAND-BOOK FOR THE MEDICAL PROFESSION PREPARED BY A SPECIAL COMMITTEE OF THE AMERICAN SOCIETY FOR THE CONTROL OF CANCER. Pp. 54, American Medical Associated Press, Chicago.

IN February, 1917, by vote of the National Council of the American Society for the Control of Cancer, a Committee was appointed to prepare the manuscript of a hand-book on cancer, for circulation among the members of the Medical Profession of the United States. This was done for the purpose of dissemination of facts in regard to cancer to the end that its mortality may be reduced by a wider knowledge of the disease. After the formulation of the essential data for this hand-book, the committee selected submitted these facts to the leading medical men of the country. In turn, their criticisms and suggestions were incorporated to the best ability of the committee in the formation of this pamphlet. The views expressed are therefore the views of the leading men of the profession throughout the country.

In this small pamphlet the urgent need of early treatment is set forth in order to reduce the mortality. Its aim is to educate the Medical Profession as well as the public in making early diagnosis and instituting prompt treatment. It sets forth the responsibility of the physician to the general public, and points out the consequence of neglect.

The various forms of cancer in the different portions of the body with symptoms and findings are correlated in a very brief manner. The various precancer conditions, as well as various cures are also given. In conclusion it is one of the greatest helps in getting this essential knowledge before the medical profession in a brief, concise manner, and one who follows its teachings will do much to decrease the mortality from this disease in his community. T. K.

MEDICAL CLINICS OF NORTH AMERICA. Volume III, No. 1, Chicago No. Pp. 277; 59 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number is entirely devoted to short clinics, presumably presented to students of various colleges in Chicago. Dr. Isaac A. Abt presents the subject of prognosis of disease in infancy and childhood, pointing out many pitfalls and many useful suggestions for the general practitioner. He also reports a case of Hanot's cirrhosis in a two-year-old child, giving history, and differential diagnosis. Dr. Frederick Tice reports a case of mediastinal tumor which proved to be a lymphosarcoma. In addition he also presents a case of carcinoma of the stomach. In both cases autopsy findings

are included, and in the latter two pieces of steel wire were found at autopsy and not discovered at the time of the roentgen-ray examination: this was probably due to a poor plate, although the wire was deeply embedded in the omentum. Dr. Milton M. Portis reports a case of carcinomatus metastases in bones secondary to carcinoma of the stomach. The patient at time of admission complained only of pulmonary symptoms and the gastric carcinoma was discovered by routine examination. He also reports a case of acute pyelitis simulating intestinal obstruction. Dr. Clifford G. Grulee points out the importance of examination of urine in children with a continued fever, stating that pyelocystitis in infancy is very frequently overlooked and is the cause of this continued fever. Dr. Solomon Strouse deals with the problem of pulmonary tuberculosis in association with other diseases in the general hospital, stating that many patients will hide their predominating symptoms in order to gain admission. He considers the differential diagnosis in cases of tuberculosis with gastro-intestinal symptoms; pulmonary tuberculosis and hyperthyroidism; diabetes and tuberculosis. One of the most important articles recorded in a case of malignant endocarditis of the pulmonary valves, with autopsy findings by Dr. Charles Spencer Williamson. He also points out the significance of the urgent search for superficial nodules in gout and the examination of these under the microscope for sodium-biurate crystals. The treatment of gout is also given in detail. Dr. Peter Bassoe gives his experience with the Swift-Ellis treatment of parietic dementia. The treatment of constipation is given in full, with diet lists appended by Dr. W. D. Sansum. He deals with the problem from a psychological and physiological standpoint, making the patient realize all factors concerned in intestinal digestion. His use of charcoal as a marker is a helpful suggestion and makes the patient realize the time required for the emptying of the intestinal tract. Dr. George F. Dick reports an unusual case of typhoid fever in which a bacillus resembling the typhoid bacillus was cultured from the urine and feces. This bacillus agglutinated the patient's own serum as well as paratyphoid A in a 1 to 80 dilution. Widal reactions were negative except with this strain of organism. The cardiac arrhythmias are dealt with by Dr. James G. Carr. He presents 4 cases dealing with the following arrhythmias: (1) premature ventricular contractions, with a history of paroxysmal tachycardia following an attack of typhoid; (2) a case of premature contraction upon an arteriosclerotic basis; (3) premature ventricular contraction in association with hypertension, also showing pulsus alternans; (4) a case of pulsus alternans occurring in a course of mitral disease. He also reports a case of pulmonary abscess following tonsillectomy. Dr. Arthur Byfield reports a case of Hodgkin's diseases. He makes a strong plea for a more precise nomenclature in the interpretation of Hodgkin's diseases. The outstanding

clinical features of the disease are given briefly in the article, special attention being given to the association of pruritus as an early symptom. The blood pictures are also reviewed in detail, many cases showing a marked leukocytosis. He is also of the opinion that Hodgkin's disease is not connected with tuberculosis.

J. K.

THE MEDICAL TREATMENT OF CANCER. By L. DUNCAN BULKLEY, M.D., Senior Physician to the New York Skin and Cancer Hospital. Pp. 386; 2 charts. Philadelphia: F. A. Davis Company.

THE book is composed of a series of short papers, which have been formerly presented to various medical societies, etc. Dr. Bulkley makes an urgent plea for the study of the cancer problem from a biochemical standpoint. He cites the increase of the morbidity and mortality of cancer in the civilized world and tries to connect this increase with our new form of living. His studies are entirely from a metabolic standpoint, in which he feels that the alterations of our diet, principally in the form of increased meats, alcohol and coffee, plus nerve strain, are the most important factors. His case reports are full and complete, he paying a great deal of attention to the quantitative analysis of all excreta, and special attention being paid to the condition of saliva and quantity of urine secreted. He reviews the knowledge gained from the laboratory in cancer research, both from a positive and negative phase, and makes strong pleas for a closer association of clinical manifestation and laboratory research. He feels that surgery is only in a sense a palliative measure, stating that 90 per cent. of those attacked by cancer, excluding epithelioma, succumb to the disease. From his case histories there must be a great deal to the metabolic theory, and undoubtedly the near future will be very bright in the cancer problem from this viewpoint. His plan of treatment with diet lists is also included.

T. K.

THE PITUITARY. By W. BLAIR BELL. Pp. 329; 7 original colored plates and 190 illustrations. New York: William Wood & Company.

THIS book, from the press of William Wood & Co., New York, is the latest and most complete work of W. Blair Bell on the subject of the hormonopoietic system. Some of the articles have been published previously as the substance of a Hunterian Lecture, delivered at the Royal College of Surgeons, and some as monographs, for one of which the author was given the Astley Cooper prize and the John Hunter medal. The earlier works by Bell were devoted

mainly to gynecological studies, his *Principles of Gynecology* and the *Sex Problem* being well known. Since 1906 his writings have been devoted more exclusively to the endocrine system.

In his one volume the author essays in systematic order a compilation of the different phases of the work on the pituitary. He discusses the morphology, physiology, pathology and surgical treatment of the organ, together with an account of the therapeutical uses of the extract of the gland. Very many useful references are given and quoted. A great deal of space is wasted in discussing, pro and con, the works of Dr. Harvey Cushing, resulting in considerable repetition of statements throughout the volume.

The author states that he regards the pituitary as "one gland," that the anterior and posterior lobes function as a unit, but the reader leaves the book inclined to the view of the dual nature of the organ.

The book sheds little new light upon the very perplexing question of the interrelationship of the pituitary to the other organs of internal secretion. Should as complete works appear upon the other glands of the hormonopoietic system a great advance will have been recorded in this direction.

As a whole the book is a very practical and important addition to the literature on the ductless glands. F. H. L.

CEREBROSPINAL FLUID. By ABRAHAM LEVINSON, Associate in Pediatrics, Northwestern University Medical School. Pp. 231, 56 illustrations. St. Louis: C. V. Mosby Company.

THE monograph as a means of gathering together the investigations and observations of an individual who has studied any particular subject or phase of a subject is always helpful. In this book, too, the literature has been quite thoroughly covered and a complete bibliography given.

The opening chapter contains an interesting history of cerebrospinal fluid. Here is shown how each improvement in medicine and each advance in bacteriology, serology and chemistry improved our knowledge of cerebrospinal fluid. The anatomy and physiology of the fluid is considered, and it is pointed out that even yet its origin is unknown. The methods of obtaining cerebrospinal fluid by lumbar puncture and cranial puncture are clearly described and illustrated. The author believes that the presence of blood in the fluid is the most common cause of the failure in lumbar puncture. The reviewer cannot quite agree with this, as it has seemed to him that pushing the needle too far in is the great temptation to the uninitiated, especially in younger children. In separate chapters the properties of normal and pathological cerebrospinal fluids are

taken up. In these chapters, and in the one on examination for diagnostic purposes, there is a complete exposition of the latest newer knowledge of the subject. All the tests are described and their values pointed out. There is a chapter in which the type of abnormality in the cerebrospinal fluid in different diseases is shown.

The book closes with a discussion on intraspinal treatment.

A. G. M.

THE SURGICAL CLINICS OF CHICAGO. Volume III, No. 5, October, 1919. Pp. 258, with 94 illustrations. Philadelphia and London: W. B. Saunders Company,

It has been the writer's good fortune to review the *Surgical Clinics* for several months past. The work has always been of the highest standard, and the present number is no exception. The profession is familiar with the list of contributors and needs no reviewer to point out their standing.

This is the first number since the recent war to approximately return to peace-time surgery. Most of the articles illustrate both the development of the diagnosis and the surgical treatment in detail.

There are many instances in which the contributor gives to the reader points in technic and methods peculiar to himself, in which difficulties we all meet are surmounted in a clever manner. These little refinements in technic are not found in text-books, which fact of itself makes the *Surgical Clinics* of great value to its readers.

E. L. E.

PAPERS ON PSYCHO-ANALYSIS. By ERNEST JONES, M.D., M. R. C. P. (Lond.), Co-editor of the International Journal of Medical Psychoanalysis; President of the London Psycho-Analytical Society; Late Associate Professor of Psychiatry at the University of Toronto. Second edition. Pp. 700. New York: William Wood & Co.

This book is the revised and enlarged edition of papers on psycho-analysis by a well-known writer on this subject. With the exception of the introduction, every one of these papers has appeared in some journal, although in many instances the material has been enlarged, the original substance of the paper, however, remaining. The book is divided into: General papers; papers on dreams, treatment, clinical papers and lastly papers on education and child study. It would be impossible to review a work of this kind. The author does not intend this as a text-book on psycho-analysis, although practically every phase of the subject is discussed.

At this date there is no use in arguing about the merits of psycho-

analysis. One either has no use for it or swallows whole everything Freud and his disciples teach. If by chance one deviates from the beaten path he will find himself in the position of Jung, who has been cast aside by all of those who believe in the orthodox faith, for in his preface Jones states there have been two important events in the psycho-analytic movement since 1912, that is since the appearance of the first edition. One is "the abandonment under the guise of pretended development of the principles of psycho-analysis on the part of Jung and some of his Swiss pupils," for it seems that Jung, according to the author, prefers mysticism to science. The second great event, of course, was the war, which, according to the author, has interfered with the progress of the psycho-analytical development. If there is one thing that the war has taught, so far as the practical application of the cure of functional war conditions is concerned, it is that cures were rapidly brought about by many means and that psycho-analysis was not at all necessary.

T. H. W.

ADVANCED SUGGESTION. By HAYDN BROWN, L.R.C.P. (Edin.),
Fellow of the Royal Society of Medicine. First edition. Pp.
327. New York: William Wood & Co.

ON page 230, in the chapter on a study in morbid growths, appears the following paragraph: "I have myself, at will, knowing how to act and what to expect, obtained unquestionable results by psychotherapy in dealing with examples of organic disease and abnormal growth which could not be exceeded by radium in similar cases."

On the next page, paragraph eight reads as follows: "I have indisputable proof of organic disorder and *the development of new growth having been originated by suggestion*. In one such case I have reversed the causative impression and the new growth has regressed and disappeared."

A further reading of this astonishing chapter denotes that the author has the belief that cancer can be cured by psychotherapy, or, as he calls it, neuro-induction. He prefers the latter to "suggestion," for neuro-induction to him implies "the accurate conveyance of reliable sensations and conclusions and their correct interpretation; it is a true sense demonstration and elucidation, both physically and mentally."

The author in his introduction to the chapter on his study in morbid growths, which contains the paragraphs mentioned above, makes the following naïve statement: "I wrote the following eight and one-half pages some time before finishing this book, and I offered it to two of the leading medical journals. It was declined—for what reason I shall probably never know; but I can only think, in all charitableness of heart, that the time was not ripe for

it." He later mentions specifically the *British Medical Journal* as one journal which refused to publish his views.

It is hardly necessary to say any more about this book on *Advanced Suggestions*. The astonishing part is that such a work as this should be put on the market by a reputable publisher, and that the author is a Fellow of the Royal Society of Medicine.

T. H. W.

THE PRACTITIONER'S MANUAL OF VENEREAL DISEASES. By A. C. MAGIAN, M.D., Ancien élève de l'Hôpital St. Louis, Paris. First edition. Pp. 205; 61 illustrations. St. Louis: C. V. Mosby Company.

It is difficult to assign to its proper place a book that does not actually enrich our literature. Dr. Magian's effort has been to present to the general practitioner (not the student nor the specialist) of Great Britain a résumé of modern diagnosis and treatment of the three venereal diseases, in order that the greatest good may follow the wave of interest and energetic efforts that the war created toward control of these diseases. Sixty-one pages are devoted to gonorrhœa, in too brief a survey of the subject, with numerous methods that are apparently more individual hobbies than generally accepted principles, such as three-gallon urethral irrigations, leeching, posterior urethral irrigation in acute anterior urethritis and rupture of prostatic abscess by massage; likewise omissions are noted; one looks in vain for the gonococcus to be described as an intracellular organism, certainly one of its greatest characteristics, while many of the commoner complications could have been less hurriedly disposed of by the exclusion of gonorrhœal rhinitis, pleurisy, myelitis, stomatitis, etc. A small chapter of six pages is devoted to chancroid. The remainder of the book, 128 pages, is a most interesting and accurate survey of syphilis, very readable and complete, and one can quickly see that the author's interest and work has been more centered here. His advocacy of a salvarsan injection as part of a venereal prophylaxis is to be commended, his sharply drawn schedule of treatment is a splendid guide, and his insistence on more attention being paid to general physical health and improved hygiene are essentials too often neglected.

A. R.

MENDELISM. By REGINALD C. PUNNETT, F.R.S. Fifth edition. Pp. 219; 52 illustrations, 7 color plates. London: Macmillan Company.

As a simple exposition of the principles of Mendelism, this book may be regarded almost as a classic. First printed fifteen years

ago, it has been translated into several foreign languages, and now appears in its fifth edition. Mendel is regarded as having founded the modern science of heredity. He studied the transmission of unit-characters from one generation to another, with the aim of learning something of the laws governing the distribution of these character in the offspring, such as absence or presence in the first generation and reappearance in the second generation. He used contrasting characters, such as tallness and shortness in plants, and found which was dominant and which recessive. The results of his experiments were published in 1865, but remained unnoticed until 1900. Since then investigators in various countries have confirmed and extended Mendel's results. In the animal kingdom nearly all the domesticated forms of mammals and birds have been used in breeding experiments, and in the human species, pedigrees of many families have been worked up. These deal principally with deformities and diseases, such as brachydactyly, presenile cataract, tylosis, epidermolysis bullosa, night-blindness and sex-limited color blindness. All except the last are transmitted by the simplest form of Mendelian inheritance, these conditions behaving as a simple dominant to the normal form. The recessive normals, *i. e.*, those offspring not affected, do not transmit the condition, and none of their descendents will have it. On the whole, comparatively little is known today of heredity in man, but as the author points out, that little is of very great significance. W. H. F. A.

THE OXFORD MEDICINE. ADVANCE PAGES, Vol. II, Part I. Edited by HENRY A. CHRISTIAN and SIR JAMES MACKENZIE. Pp. 149. New York: Oxford University Press, American Branch.

PART I, Vol. II, of the *Oxford Medicine*, offers to its subscribers the best pages so far issued to them. The major portion is devoted to diseases of the heart, by Sir James Mackenzie. Now that Osler has gone "to his long home," Mackenzie remains as the other great personality in English medicine. These pages epitomize much for which he will be remembered and contain many ideas which this master physician has emphasized for the profession. Characteristically Mackenzian are the lines devoted to pointing out the importance of the heart muscle over against all other things in the prognosis and treatment of cardiac disease. In this section, too, are to be found the deprecation of the importance which has been attached to heart murmurs. Of course, he pleads for careful clinical study in preference to studies gained by instruments of precision—not that he fails in appreciation of these aids. Further than this, he calls attention and substantiates his claims for the uselessness of mathematically trying to determine cardiac power. Some of the best

portions of this superlative section are devoted to the soldier's heart, and one must agree that all is said that can be said of this peculiarly interesting condition.

One finishes Mackenzie's lines with a feeling that he should have written more of the things a rich life has revealed to him. The whole discussion exhibits a great cardiologist—really the pioneer and dean of this group of specialists—but above all does it show a great doctor?

The remaining pages of this Part I are given to two chapters on the allied subjects of bronchial asthma and hay fever, by I. Chandler Walker. The question of anaphylactic relationship to these diseases is taken up in interesting and practical detail. The determination of protein sensitivity, the specific and non-specific protein treatments as well as operative measures are discussed for those who are interested in the newer thought concerning the treatment of these usually therapeutically resistant conditions. The combination of diseases of the heart, bronchial asthma and hay fever, as discussed in this recent number of the *Oxford System*, makes it easily the most appealing one thus far sent to its subscribers. T. G. S.

AMERICAN ILLUSTRATED MEDICAL DICTIONARY. Edited by W. A. NEWMAN DORLAND, M.D. Tenth Edition. Pp. 1201; 331 illustrations, Philadelphia and London: W. B. Saunders Company.

THIS tenth edition of a well-known medical dictionary is said to be thoroughly revised and enlarged. The general plan of the book has been maintained, but many definitions and descriptions have been considerably amplified. It is said to contain over two thousand new terms. The terms are those used in medicine, surgery, dentistry, pharmacy, chemistry, veterinary science, nursing, biology and kindred branches, with new and elaborate tables. The edition appears bound in flexible leather, printed on good paper, and will be a valuable addition to any physician's library. T. G. S.

HUGHES'S NERVES OF THE HUMAN BODY. BY CHARLES R. WHITTAKER, Senior Demonstrator of Anatomy, Surgeons' Hall, Edinburgh. Second edition. Pp. 76; 12 plates. New York: William Wood & Co.

THIS is a brief statement of the bare facts about the cranial, spinal and sympathetic nerves, accompanied by schematic illustrations. It is probably intended for student use as a review book, and its brevity will be appreciated by all wishing a condensed account of the subject. W. H. F. A.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Occurrence of Unsuspected Involvement of the Central Nervous System in Selected Cases of Syphilis.—FILDES, PARNELL and MAITLAND (*Brain*, 1919, xli, 255). The material studied by the authors consisted of 624 patients with syphilis. The majority were in the early stages. Definite pleocytosis was present in 18 per cent., and in 12 per cent., from 6 to 9 cells were present in the cerebrospinal fluid. A positive Wassermann reaction was present in the cerebrospinal fluid in 6 per cent. Objective neurological findings were present in 8 cases out of the 99 in which a systematic neurological examination was made. Ophthalmoscopic changes were present in 30 of the 53 cases showing pathological changes in the cerebrospinal fluid. In 71 cases of primary syphilis in the negative Wassermann period, in which the cerebrospinal fluid was examined there was a definite pleocytosis in two instances and in 9 cases the cell increase was on the border-line. Thus central nervous system involvement may occur before serological examination reveals the presence of syphilis. Of 168 patients with primary lues but with a positive blood Wassermann, 15 showed a definite pleocytosis and in 17 the results were doubtful. The authors have thus demonstrated clearly that cerebrospinal involvement often occurs very early in luetics.

The Production of Bright's Disease by Feeding High Protein Diets.—L. H. NEWBURGH (*Arch. Int. Med.*, 1919, xxiv, 359). Reasoning from the effect of varying doses of mercuric chloride the author postulates a relationship between the concentration of substances excreted by the kidney and the renal injury thereby produced. This theory he tests

by feeding high protein diets to rabbits. Egg white and casein caused albumin and casts with definite anatomical changes in the kidney. Carefully controlled experiments were carried on over long periods with soy beans, a vegetable food substance containing a complete maintenance diet relatively high in protein. The animals on ordinary diet showed no abnormalities clinically or pathologically, but those fed soy beans developed albumin and casts and definite nitrogen retention, as high as 176 mg. of urea. On section the latter group showed acute or chronic nephritis in every instance, with a picture often very similar to the human "contracted kidney." Chronic urea administration in amounts equivalent to those excreted by the soy bean rabbits did not produce any of the results mentioned above, nor was the extent of renal injury relative to the nitrogen metabolism. Soy bean, for example, was injurious with a daily nitrogen excretion indicating an absorption of 10 gm. of protein while casein at that level was harmless but became toxic at 15 gm. per day. The author feels, therefore, that the kidney injury produced by increased protein ingestion depends on type as well as quantity.

The Control of Acidosis in the Treatment of Diabetes. — STILLMAN (*Arch. Int. Med.*, 1919, xxiv, 445) cites the methods employed at the Rockefeller Institute for early detection of acidosis in diabetes, outlines the treatment and gives examples. The symptoms of acidosis are mentioned, but reliance for the detection of acidosis is put on the plasma bicarbonate CO_2 ; blood sugar estimations being always done on the blood drawn for the CO_2 . Diabetics are divided, according to their tendencies to develop acidosis, into four groups and the criteria for classification and treatment of each group given: Group I: No tendency to acidosis either on fast or ordinary diet regardless of degree of glycosuria. Treatment: Made aglycosuric without danger by continuous fast. Usually tolerates a high calory diet without glycosuria or ketonuria. Prognosis best in this group. Group II: Received in condition of moderate or severe acidosis (plasma bicarbonate CO_2 below 40 vol. per cent.), which clears up on fasting. Treatment: Made aglycosuric without danger by continuous fast. A tendency toward acidosis is present. Safely tolerated maintenance diet to lower than that in Group I. Group III: Tendency to slight acidosis (subnormal plasma bicarbonate CO_2) on any but the most carefully chosen diets. Acidosis is not increased by fasting. Treatment: Glycosuria is removed by continuous fasting. The tolerated maintenance diet is variable. Usually acidosis becomes acute on any improper diet. Group IV: Either develop or retain severe acidosis (plasma bicarbonate CO_2 below 30 vol. per cent.), when fasted to glycosuric state. This acidosis is quite severe and becomes fatal unless the fall in the plasma bicarbonate is checked. The fall in the plasma bicarbonate is checked as follows: (1) Sodium bicarbonate, 3 gm., in cold water every hour is given until the plasma bicarbonate CO_2 is normal. (2) Fluids are forced to 5000 c.c., unless nausea contra-indicates. (3) Very strong coffee as much as 1200 to 1500 c.c. in twenty-four hours is given. (4) Catharsis with calomel and salts, and colon irrigations until no fecal matter returns. The diet is continuous fast unless with the above treatment acidosis increases then protein, such as, eggs and lean meat

to the amount of 600 to 800 calories is given. Whisky is not used. Nausea is to be scrupulously avoided as it makes treatment impossible. Fasting may be used intermittently. The tolerance is tested after the patient has become sugar-free with green vegetables alone.

Result of Treatment of Neurosyphilis (General Paresis and C. N. S. Lues); Report of Patients' Condition Four Years or More after Leaving Hospital.—SOLOMON (*Boston Med. and Surg. Jour.*, 1920, clxxxii, 60). This report deals with 10 cases of neurosyphilis, 9 of which were committed as insane. An abstract of the data is impossible in a short space. The report is of unusual interest and warrants close study. The author concludes: "The majority of cases of syphilis of the nervous system, whether so-called cerebrospinal syphilis, tabes dorsalis, general paralysis or other forms, are entitled to treatment, and if this is done thoroughly, intensively and systematically the results will be gratifying. The form of treatment, mercury, iodide, arsenic, intraspinal and intracranial injections, and the amounts, will necessarily depend upon the condition of each individual patient."

The Electrocardiogram and Ventricular Preponderance.—CARTER and GREENE (*Arch. Int. Med.*, Chicago, 1919, xxiv, 638). The authors reemphasize the fact that while the physical findings on clinical examination or the roentgenogram will furnish accurate evidence with regard to changes in the size of the heart as a whole, they afford but meager data as to the role played by the different chambers of the heart in this hypertrophy. Such data can only be secured from the electrocardiogram for the form of the latter is conditioned by the relative mass or preponderance of the two ventricles. It is furthermore pointed out that this determination of the ventricular preponderance may be done quantitatively by the calculation of the direction of the electrical axis of the heart (a) alone, for the index suggested by White and Bock for the determination of ventricular preponderance is shown to be theoretically unsound. The validity of the use of a as a quantitative guide to ventricular preponderance is shown by means of the experiments of Lewis and Cotten in which the actual weight ratio between the two ventricles was determined. Excellent agreement was found between the value of a and this weight ratio.

A Study of Pneumococcus Carriers.—SAILER, HALL, WILSON, MCCOY (*Arch. Int. Med.*, 1919, xxiv, 600) studied the incidence of pneumonia in one infantry battalion at Camp Wheeler. There were in all 90 cases of pneumonia. The minimum number of tents occupied by the battalion was 119. Sixty per cent. of the cases occurred in tents reporting more than one case. With but few exceptions the type of pneumococcus was the same for any one tent. From these facts they concluded that carriers must play an important part in the spread of pneumonia. They then studied 700 men of this regiment to find out the number of carriers. Of these 16 per cent. harbored pneumococci. Over 3 per cent. showed pneumococci of one or the other fixed types and 12 per cent. were carriers of type IV pneumococci. All these men (111 in all) were placed in wards in the hospital in various groups, and attempts were made by various means to rid them of pneumococci.

Solutions of phenol (phenol 3 per cent. in albolene) and iodine (5 per cent. in albolene) were the most valuable. These were applied as throat swabs and also dropped into the nostrils each day. They believe that in epidemics of pneumonia or of other diseases complicated by pneumonia that their methods of detecting and sterilizing carriers would be practicable and valuable.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

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Factors of Safety in Prostatic Surgery.—MELTZER (*New York Med. Jour.*, 1919, cx, 842) says careful preliminary studies are very essential when men of advancing years need surgical relief for urinary obstruction as the result of hypertrophy and intrusion of the prostate. There is always ample time to find out whether the patient can withstand the effects of anesthesia or the shock attending prostatectomy. Many lives can be saved by a two-stage operation, with careful nursing and strict attention to improving the kidney function. The usual physical examination alone cannot tell when the favorable stage for the second operation has occurred. It can be ascertained only by a routine examination and careful study and analysis of the following: (1) The appearance of the tongue; (2) the blood chemistry; (3) the kidney function by the phenol-sulphonaphthalein test; (4) the patient's general condition; (5) (a) the roentgen-ray examination of the entire genito-urinary tract; (b) the results of a cystoscopic examination; (c) a complete urinalysis, preferably of a twenty-four-hour specimen; (d) the presence of residual urine; (e) a twenty-four-hour measure of fluid intake and output. Meltzer thinks the first four examinations are the determining factors as to whether or not a prostatectomy can be done, and he terms these factors the factors of safety.

Deformities of the Hand.—GILL (*New York Med. Jour.*, 1919, cx, 1061) says that deformities of the hand may be either congenital or acquired. The congenital deformities are club-hand, contracture of the fingers, syndactylism, polydactylism, partial or complete suppression of the fingers and hypertrophy of the fingers. In cases of syndactylism the best results are secured by plastic operation, in which the skin from the dorsum of one finger is used to cover entirely the skin defect in the other finger, and in which a flap from the dorsum of the hand is employed to cover the raw surface of the first finger. The acquired deformities of the hand comprise the various forms of club-hand and deformities of the fingers. Club-hand may be due to: (1)

Curvature of the bones of the forearm from disease or from fracture; (2) defect in the bones of the forearm; (3) Madelung's deformity of the wrist; (4) destructive disease of the bones of the wrist and carpus; (5) certain paralytic and muscular conditions; (6) burns of the wrist and forearm as well as infections and injuries. Acquired deformities of the finger may be classified as follows: (1) Contractures which are of cicatricial origin involving the skin only; (2) contractures of fascial origin—Dupuytren's contracture; (3) deformities of the fingers due to affections of the tendons; (4) contractures of the fingers resulting from lesions which have destroyed more or less of the muscle substance of the flexor or extensor of the fingers; (5) various forms of arthritis, osteoarthritis and gout; (6) nervous disorders, such as spastic paralysis, infantile paralysis, obstetrical or birth palsy and the definite nerve palsies. (7) Deformities arising from disease of the bones, such as syphilis, tuberculosis and tumors. Gill thinks that the two deformities of the hand of greatest practical interest are those due to Volkmann's contracture and to malunion of Colles's fracture. The cure of Volkmann's contracture is extremely difficult. The best results are to be obtained by complete dissection of the muscles involved, whereby they are freed from one another and from the overlying and underlying tissues. This dissection should be followed by implantation of a free fat transplant to prevent readhesion. Another almost equally disabling deformity of the hand may follow Colles's fracture. Many persons who have suffered a Colles's fracture are unable to resume active work for many months or even years. The cause of the disability is the stiffness of the hand and the fingers, which prevents the grasping of objects, and is frequently accompanied by a swelling and coldness of the hand. Gill considers this condition due to improper reduction of the fracture. He also says that it is impossible by roentgen-ray examination to tell, absolutely, whether or not a good result will be obtained. If the swelling and other signs of interference of circulation persist beyond the first week the surgeon should consider an open operation.

The Choice of Method in Operations upon the Pituitary Body.—FRAZIER (*Surg., Gynec. and Obst.*, 1919, xxix, 235) says that in its pathological deviations the pituitary is very similar to the thyroid. Both glands have as their most common pathological lesion the adenoma, often cystic in character. Seventy-five per cent. of pituitary tumors belong to the adenomata. The symptomatology falls into various groups: (1) Those due to general intracranial pressure, such as headache; (2) those due to involvement of the optic tract and chiasm, such as the ocular hemianopsia; (3) those due to involvement of neighboring structures; (4) those due to disturbances of internal secretion. Only two methods of approach are of use to the surgeon: first, the submucous septal approach of Hirsch and Cushing, and second the authors' fronto-orbital method. In analyzing these two methods from the standpoint of (1) safety and practicability, (2) degree of exposure and (3) end-results, Frazier believes the fronto-orbital route to have the wider field of application. The mortality of the submucous septal method is 9.4 per cent. while that of the fronto-orbital method is only 6.4 per cent. Meningitis is the cause of the majority of fatalities by the submucous septal approach.

Frazier considers those pituitary tumors which are primarily and exclusively intracellular at the time of operation as suitable for the nasal method. It is, however, often impossible to determine either by symptoms or roentgen-ray examinations whether the tumor has extended beyond the sella turcica or whether it was primary at this site. Degenerative optic phenomena and signs of increased intracranial tension are strong arguments in favor of the author's method of approach. Since many of the cases show the sphenoid sinus to be partially or wholly obliterated the improvement by the septal approach will be of short duration. Furthermore, since 19 per cent. of pituitary adenomata develop cysts, evacuation by puncture is of only transitory benefit. Removal of a portion of the cyst wall, however, can be done by the supracellular route. The author has modified his original approach so that now it is intradural instead of extradural, and this is clearly illustrated by twelve illustrations.

Snapping Hip.—MAYER (*Surg., Gynec. and Obst.*, 1919, xxix, 425) reports 4 cases that have come under his observation. All 4 cases were associated with some abnormality of the fascia lata, which caused it to catch back of the great trochanter. Mayer thinks that the cases of snapping hip due to irregularity of the acetabulum which allows a subluxation to take place are exceedingly rare. Zur Verth was the first to call attention to a normal thickening of the fascia lata running longitudinally from the iliac crest downward just in the line of the posterior margin of the great trochanter. He called this the *tractus cristo femoralis*. Any condition which causes abnormal thickening of the *tractus cristo femoralis*, or unusual prominence of the trochanter, or an abnormal relaxation of the *gluteus maximus* muscle, may be the responsible factor. The non-operative treatment consists in preventing the fascia from catching in back of the trochanter. Firm pressure back of the trochanter, to prevent adduction, which is the initial step in the production of the snap, is useful. This can be exerted by adhesive plaster or felt, or by a mechanical contrivance. Relaxation of the *gluteus maximus* can be overcome by adhesive straps or by a firm flannel spica bandage. The principle of the operative treatment is to divide the *tractus cristo femoralis* and suture it in such a way as to prevent it forming again.

Joint, Nerve and Other Injuries in War Surgery.—JONES (*Surg., Gynec. and Obst.*, 1920, xxx, 1) says that experience taught the English surgeons to explore peripheral nerve injuries earlier and more frequently than they did at the beginning of the war. In cases which do not spontaneously recover in a month or two it is a mistake to await regeneration of the nerve and an exploratory operation should be undertaken. Inspection of the exposed nerve at the time of operation and its faradic excitability should be regarded as a part of the diagnosis. It is important to approach the nerve through normal tissue and not through scar tissue. Nothing is to be gained by surrounding the suture line with vein or cargile membrane. Bridging the defect by catgut, vein, alcoholized nerve or turning down flaps of nerve tissue has been disappointing. End-to-end suture by a one- or two-stage operation is the method to be adopted in every case. More systematic and thorough education is

required in the treatment of fractures. This can only be obtained by setting apart wards for fractures under the care of men who devote real interest to the subject or by retaining certain institutions solely for the treatment of these cases. Gunshot injuries of the femur were "the tragedy of the war." The mortality from fractured femurs, according to Gray, who collected statistics over one of the army areas in 1916, amounted to almost 80 per cent. In 1918 Bowlby reported the mortality in field ambulances and in casualty clearing stations was reduced to less than 20 per cent. This dramatic change was due first and foremost to the proper use of the Thomas splint. Jones has taught that fracture of the femur, simple or compound, treated by a Thomas splint, should, at the worst, not yield more than half an inch of shortening; secondly, it was due to a subjugation of sepsis and gas gangrene, and, thirdly, to those accessories which prevented or lessened shock. The caliper splint should be used for some months after apparent union is procured in order to prevent angulation. In recent and in ancient fractures all joints should be kept mobile and the muscles should be regularly stimulated by electrotherapy. The restoration of functions in joints is too vast a subject to dwell upon. Forceful movements are rarely indicated. If pain occurs after manipulation and is of short duration movements may be continued. If pain persists for lengthy periods after manipulation rest is indicated. If the increased range of movement is maintained after manipulation further movement can be safely prescribed. If in spite of movements, even in the absence of great pain, the range is continually diminishing, rest is indicated.

THERAPEUTICS

UNDER THE CHARGE OF

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Severe Dermatitis during Treatment with Novarsenobillon.—LEONARD (*British Med. Jour.*, December 13, 1919, p. 773) reports a case which illustrates the risk attending the use of novarsenobillon. The patient was a soldier, aged twenty-three years, suffering from secondary syphilis. Three injections of 0.45 gram novarsenobillon and 1 gram mercury were given intravenously at weekly intervals. No reaction occurred until the fourth week of treatment, when, two days after the last injection, dermatitis and symptoms of toxæmia developed. The condition did not entirely clear up until about two months after onset. The points of interest in this case are: (1) The occurrence of a severe dermatitis and toxæmia after the administration of only 1.9 gram of novarsenobillon. (2) The high temperature recorded, 105° F. (3) The

simultaneous occurrence of three distinct types of eruption: maculopapular, scarlatiniform and urticarial. (4) The marked general adenitis at the onset, present before the lesions, other than the scalp, had become pustular. (5) The negative Wassermann reaction of October 8; that on July 24, before treatment commenced, being strongly positive.

A Clinical Analysis of Influenza Cases.—BLUMGARTEN and VOSS (*New York Med. Jour.*, January 24, 1920, p. 146) give the following conclusions regarding the recent (1918) pandemic of influenza. The severe cases were complicated by pneumonia, usually bronchopneumonia. They did not find the influenza organism in the blood or sputum in most of the cases (over 100) examined. Most of the severe cases, complicated with pneumonia, showed a distreptococcus in the sputum resembling the *Streptococcus hemolyticus*. They believe that the pneumonia was due to an infection with a secondary organism, such as the streptococcus or staphylococcus, the infection with the former type of organism usually being fatal. A persistent temperature of 105° F. or over was usually a bad prognostic indication. The white blood cell and differential counts were the best prognostic signs. A leukopenia and high polymuclear count usually meant a bad prognosis. The three principal causes of death were (a) cardiac failure; (b) acute pulmonary edema; (c) hemolysis. The autopsy findings showed evidences of general infection, with parenchymatous degeneration of the viscera and infarcts in the spleen and other viscera.

A New Germicide for Use in the Genito-urinary Tract—"Mercurochrome-220."—YOUNG, WHITE and SWARTZ (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1487) give a preliminary report of experiments and clinical studies with mercurochrome-220 in genito-urinary infections. They conclude that: (1) Mercurochrome-220 is experimentally a drug of great germicidal value, a solution of about 1 to 1000 killing *Bacillus coli* and *Staphylococcus aureus* in urine in one minute. It has practically fifty times the germicidal strength of acriflavin in urine medium for exposures of one hour. (2) In a strength of 1 per cent. the new drug is tolerated by the human bladder for from one to three hours without irritation. Injections of 1 per cent. solution into the renal pelvis are likewise free from pain even when held *in situ* by plugging the catheter. (3) That mercurochrome-220 has a remarkable germicidal value is shown by the rapid sterilization accomplished in a series of cases of cystitis and pyelitis of long standing and refractory to other treatments. The rapidity with which a few cases of old, purulent cystitis disappeared was surprising, becoming free of pus and bacteria in a few days. (4) Studies of the comparative value of acriflavin and mercurochrome-220 in gonorrhoea are not yet complete, but it has been demonstrated that with both drugs methods of great value in the treatment of the disease have been produced. (5) Mercurochrome-220 has proved to be eminently satisfactory in the treatment of chaneroids and as a dressing for buboes after incision. Other drugs developed along the same lines have been produced and are being experimented with by them.

The Specific Treatment of Hay Fever.—RUCKEMANN (*Boston Med. and Surg. Jour.*, 1920, clxxvii, 295) says that the results of treating 91 cases of fall (rag-weed) hay fever was as follows: Nearly 9 per cent. of patients were entirely freed from their symptoms; 62 per cent. were moderately relieved. Of the remaining 28 per cent., about one-third showed no relief at all. The best results were apparently obtained with a moderate amount of specific treatment, since in these cases even after considerable preparation the tolerance for rag-weed pollen extract still remains at a very low level. Systemic reactions occurred after 2 per cent. of individual injections and were not always due to an overdose. The author believes that in view of the fact that so few of the postulates of experimental anaphylaxis hold good of hay fever, it is probable that hay fever depends on a mechanism which is not anaphylactic but which is perhaps closely associated with that of drug idiosyncrasies.

Acidosis in Nephritis.—CHACE and MYERS (*Jour. Am. Med. Assn.*, 1920, lxxiv, 641) state that the subject of acidosis in nephritis is one of such practical importance that it deserves emphasis from the clinical point of view. They cite observations on acidosis in nephritis in 20 fatal cases, all showing marked nitrogen retention. They found in all a severe acidosis, sufficient in many instances to be the actual cause of death. The part played by acidosis in clinical symptoms of so-called uremia is difficult to tell. Patients with pronounced acidosis present a somewhat different clinical picture from that of uremia. They were able to obtain quite definite clinical results by infusions of sodium bicarbonate solutions. They advocate the determination of the degree of acidosis by the determination of the carbon dioxide combining power of the blood plasma by the Van Slyke method, which method, furthermore, should control the administration of the alkali. They found that in certain cases of acute nephritis and acute exacerbation of chronic nephritis the distress was apparently due to the acidosis, since the judicious use of sodium bicarbonate resulted in general clinical improvement. With the rise in the carbon-dioxide-combining power of the blood the dyspnea and hyperpnea disappeared.

Sodium Chloride Diuresis.—POLAG (*Schweiz. med. Wchnschr.*, 1920, i, 29) calls attention to the fact that sodium chloride has long been known as a powerful diuretic, and he has used it for this purpose as a last resort in advanced nephritis. He confines its use practically to desperate cases. He gives a few cases showing striking benefit following a period of considerable times on a salt-free diet. He believes that when no benefit has been realized from the salt-free diet, giving a single large amount of salt during one day or three days during the week, may induce such a diuresis that considerable clinical improvement results. He states that we have no means of knowing at present which cases will respond favorably to this plan of treatment and which will be aggravated by it. Its use is comparable to the ingestion of large amounts of water used as a diuretic in kidney insufficiency.

PEDIATRICS

UNDER THE CHARGE OF

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The Deleterious Effect of the Alkalinization of Infants' Food.—Hess and Unger (*Jour. Am. Med. Assn.*, November 1, 1919) call attention to the fact that little attention is paid to the reaction of the milk preparations fed to babies. Their attention was attracted to this question by their experience that milk formulas containing malt soup had an unusual tendency to bring about scurvy in infants unless an antiscorbutic such as orange-juice or canned tomato was added to the dietary. They think that the undesirable effect is brought about by one or more of the following conditions: that the formulas contain an amount of milk insufficient to protect fully; that the preparation is boiled as well as frequently prepared from pasteurized milk; that there is a period of incubation between the initial pasteurization and the boiling of the milk and flour; that an alkali is contained in the malt soup; and that a considerable amount of carbohydrate in the form of flour and of malt sugar is added to the food. They point out also that it is by no means immaterial whether the food is rendered more or less alkaline. It is impossible to say what effect an addition of alkali has on protein and other caloric food factors at the present state of knowledge. This alteration surely has a decided effect on the vitamins. They have shown in a previous article that orange-juice, the prototype of antiscorbutics is essentially damaged within twenty-four hours by being rendered twentieth normal alkaline to phenolphthalein. It was found that orange-juice of this faintly alkaline reaction had lost its power to protect guinea-pigs against scurvy. The antiscorbutic vitamin is peculiarly sensitive to alkalinization. This vitamin seems to be more sensitive to various physical and chemical influences than either the water-soluble or the fat-soluble vitamin. There is at present some difference of opinion as to the vulnerability of the water-soluble vitamin to the application of heat in an alkaline medium. The results of the authors have an application far wider than their application to malt soup. Investigation showed that alkaline potassium salt was added to the greater number of our proprietary foods for infants. There are two reasons for this, namely: it renders the food less subject to acid fermentation, and because the addition of potassium counterbalances the relative poverty of this salt in cow's milk. It is added in from 2 to 2.5 per cent. in the form of the bicarbonate of potassium. They suggest that the citrate of potassium could be substituted in these foods without giving rise to this danger of scurvy as is the case of the alkaline salts, except where the addition of the alkaline salt must be used in order to change the reaction from acid. They say that cod-liver oil is rich in the fat-soluble vitamin, and that it is almost a specific in the treatment of rickets.

Diabetes in Infancy and Childhood.—**ABT** (*Endocrinology*, July-September, 1919) says that diabetes in children is infrequent as compared to diabetes in adult life. In the first fifteen years of life boys are more frequently affected, and both sexes show an equal frequency from five to ten years. Heredity has an influence but the author found such only occasionally. Trauma plays a part in causing diabetes. There is no clinical or pathological basis for the assumption that infectious diseases are a cause. No cases have been reported in the literature in which a relationship exists between lesions of the hypophysis and diabetes in children. Lipemia occurs frequently in diabetes. The symptoms are almost identical with those in adults such as loss in weight and strength, fatigue upon slight exertion, increased appetite, polydipsia and polyuria. Enuresis frequently occurs. Urticaria, pruritus, and eczema occur as well as furunculosis. The teeth decay early and stomatitis is not uncommon. Edema of the face and ankles have been seen in advanced cases. Headache, backache and radiating pains in the extremities are sometimes seen. Particularly characteristic are the pains in the calf muscles. The urine contains sugar, and at times acetone and diacetic acid and not infrequently albumin and casts. It may be either mild or severe and sometimes the transition from the mild to the severe form occurs more rapidly than in adults. Some children seem to improve after the sugar tolerance is established and urinary sugar kept low. The sugar returns on the slightest provocation such as disappointment from a bad school report and also following coryza, parotitis, pharyngitis and diarrhea. Usually the sugar tolerance can be restored, but succeeding recrudescences tend to reduce the level of the tolerance.

Psychopathic Clinic of the Children's Court of the City of New York.—**MONTAGUE** (*Mental Hygiene*, October, 1919) has studied 268 cases of recidivists with the result that she found that 82.9 per cent, with one previous court record were mental deviates and 24.5 per cent. of this number were feeble-minded. Of those with three or more court records 90.9 per cent. were mental deviates and 48.5 per cent. of this group were feeble-minded. In addition to the fact that mental deviation is such a high percentage, it is recognized that many criminal careers are due to repeated exposure of these individuals to unfavorable environment. Among the cases brought up to the clinic this stood out prominently. Of the cases studied 170, or 63.4 per cent., were found to have unfavorable environment.

The Role of the Pineal in Pediatrics.—**GORDON** (*Endocrinology*, October-December, 1919) says that it is generally accepted that the greatest postnatal development in the pineal gland is in the first few years of life, and that it is at all functionally active, it is at this period. Some believe that the pineal produces a secretion which inhibits the growth of the body and restrains mental and sexual development from exceeding the rate accepted as normal for pre-adult life. This inference arises from the occurrence of the sexual and physical precocity accompanying the invasion of the pineal gland, and that the resulting metabolic and neurological disturbances occur from lack of pineal secretion. Others claim that the symptoms of sexual and physical precocity are due to hyperpinealism instead of to a diminished secretion. It is

exceedingly difficult to arrive at any conclusive opinion as to the function of the pineal gland. There has been nothing substantial brought forward to show that it possesses a function and no experimental studies are so complete as to allow comparison with the very striking syndrome seen clinically.

Early Synostosis of the Epiphysis with Dwarfism in Pubertas Precox.

—KRABBE (*Endocrinology*, October–December, 1919) reports a case of a girl, aged thirteen and a half years. Bleeding from the vagina began when she was only a few months old, and has recurred regularly every four weeks since that time. The breasts were always prominent, but it was noted that they were most prominent from her sixth to her seventh years. After that time there was a diminution in size, and now they have the appearance of the breasts of a middle-aged virgin. For two or three years a growth of hair in the axilla and over the pubis was noticed. Her hips and thighs have always been large. She grew rapidly in height until she was seven years of age. Since that time growth has stopped. The lower limbs are strikingly short in relation to the trunk. Roentgen-ray showed a normal sella turcica. All of the epiphyseal fissures of the lower and upper limbs were completely grown together. The girl has a childish face and has given no evidence of any sexual knowledge in spite of the marked development of menstrual function and external evidences of sexual maturity. For this reason no intravaginal examination were made, so that the reporter was unable to eliminate the possibility of an ovarian abnormality being the cause of the condition. This type of dwarfism is in characteristic contrast to that which is found in thyroid and pituitary diseases. In these the epiphyseal fissures remain barely open, but for an abnormally long time.

Bone Deformities of Renal Dwarfism.—BARBER (*Lancet*) says that

in the last few years a number of cases of interstitial nephritis in children associated with stunted growth have been recorded, some of them with infantilism in all of its characteristics, others with merely a marked degree of dwarfism. It is not easy to select a name for this condition, but as the kidney disease not infrequently has a very insidious onset, and many of the cases seek advice for the first time because of retardation of development, or for bone deformity, some name such as renal dwarfism may be used. Out of 8 cases 5 have shown bone deformity, but this does not enable one to discuss the percentage, because 4 of these 5 first sought advice for genu valgum. The signs and symptoms are more or less latent, and there may be cases of interstitial nephritis, which are never diagnosed at all. The deformities appear to develop about the time of puberty. The genu valgum appears to develop comparatively quickly, straight legs becoming markedly deformed in a few weeks. In type the changes seem to be very similar to those of rickets, the wrists and knee-joints being most noticeably affected, but some swelling is often palpable at the junctions of the ribs and costal cartilages. Roentgenologically the most marked changes are seen at the wrists and the knee-joints, there being an increase in size of the proliferation zones, and the normal translucent line is greatly increased in breadth. There is not only enlargement, but also great irregularity and

want of definition due to irregular calcification. In this article there are reported 3 cases which show these signs and symptoms. One of these cases has since died as a result of uremia. Postmortem the kidneys were found to be very small and fibrotic. Microscopically there was a very marked interstitial nephritis.

GYNECOLOGY

UNDER THE CHARGE OF

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Effect of Radium on Cervical Cancer.—A very extensive study of the histological changes in squamous-cell carcinoma of the cervix of the uterus after radiation has been made by ALTER (*Jour. Med. Research*, 1919, xl, 241) during the course of which he determined that the so-called "squamous"-cell carcinoma of the cervix is a basal-cell growth, having three types: Solid, adenoid and cystic. The primary effect of the rays of radium in the case of the basal-cell carcinoma of the cervix is the destruction of the cells of the malignant parenchyma. The increase of stroma is secondary, due to the disappearance of parenchyma, having been formed mostly from wandering cells. Cell divisions, even if probable, are not primarily important. In his long series of histological investigations, invariably the chromatin substance of the parenchyma cells displayed the greatest sensitiveness toward the rays of radium, showing conspicuous features of destruction while the protoplasm of the parenchyma cells showed marked but not such obvious changes. Alter believes that the changes of the protoplasm and the nature of the infiltration seem to suggest the different stages of deep-seated chemical changes, due to the action of the rays of radium.

The Cystic Ovary.—A moderate acquaintance with the cystic ovary, gleaned through serious and earnest attention whenever the condition was encountered during an abdominal section, has led REDER (*Am. Jour. Obst.*, 1919, lxxx, 719) during latter years into a different channel of reasoning relative to the treatment of this condition, from which he entertained during former years. The cystic ovary, which is being considered in this article, is not the organ which has suffered from a microbic invasion; but the organ which, through adverse influences, reasonably assumed to be mechanical in their nature has suffered changes in its stroma and epithelial structure that have carried it beyond recognized physiologic limits. Furthermore, this argument is confined to ovaries belonging to unmarried women, ranging from fourteen to

twenty-five years, where the cystic degeneration was discovered during an abdominal section performed for a lesion not in any way associated with the ovary. In those instances in which resection of the ovary was decided upon the guiding principles were the large number of cysts present. An ovary which showed a moderate amount of cystic degeneration was not resected; but a prolapse or faulty position of the uterus was invariably corrected, and the future fate of the ovary trusted to the correction of the displaced uterus. When during an abdominal operation an ovary is encountered which presents on its surface from five to eight cysts, varying in size from a pea to a small hazel nut, the author believes the ovary is pathological and is a proper one for resection. It is logical, he believes, to infer that in instances of this kind, many more cysts are imbedded deeper down and throughout the glandular substance of the ovary, and that their presence creates a pressure atrophy of the functional elements with the concomitant inhibitive efficiency of the organ. Simply puncturing these cysts and evacuating the light, thin serous fluid, which may, in some cases, be brownish or blood-stained, is a procedure of little promise for an ovary in which cystic degeneration has gone beyond the physiologic limits. This procedure is not to be recommended for cysts projecting above the surface of the ovary, as it carries with it no assurances of good. The smaller cysts, grouped deeper in the glandular substance, where removal during resection is not deemed advisable on account of the great sacrifice of healthy ovarian tissue, may be punctured because the cyst is small, its walls delicate, and furthermore, because it is the only surgical measure permissible. As a result of his investigation into this subject, the author concludes that without an abnormal position of the uterus, be it a retrodeviation or a descensus due to ligamentous relaxation, there is seldom a prolapsus of the ovary; without prolapsus of the ovary, there is no abnormal hyperemia; and without an abnormal hyperemia, cystic degeneration of the ovary is rare.

Treatment of Tubal Infection.—Having analyzed the case records of 1000 patients who were operated upon at the Cook County Hospital for tubal infection, WOOLSTON AND WHITE (*Surg. Clinics*, Chicago, December, 1919, p. 1495) state that the end-results are very discouraging in those cases in which conservative surgery has been practised, since many of the patients must return for further treatment. Of course it is always desirable to attempt to save the ovaries especially in young women, on account of the value of the internal secretion of the ovary, but they do not think that it is advisable to preserve *diseased* ovaries even in young women, as they are so liable to give trouble later. They would divide the treatment of chronic pelvic infections into the conservative and the radical, the choice of treatment depending upon the social condition of the patient to a great extent. If a person is well to do, rest in bed, good nursing and general hygienic measures will cure many cases. These cases can well afford to risk a certain number of acute exacerbations in the hope that spontaneous healing may occur and operation be thus avoided. With the less fortunate patient who cannot afford to be sick, because she is employed or because she must go to a charity hospital where beds are limited, operation is indicated sooner. Also, if a patient has a family of children or is beyond the

climacteric she may submit to a radical operation; whereas a patient who has no children but who is within the childbearing age and desires motherhood can afford to take conservative measures over a longer period of time, hoping that nature will heal the tubes so that conception may take place. If operation has been decided upon, which, of course, is never during an acute attack, one should be sure to remove all the pathological tissue, which is so often only partially removed. In the gonorrhoeal form the infection is practically always in both tubes as well as the *pars interstitialis*. This means a hysterectomy or an amputation of the uterus, which is sometimes called a Bell-Beuttner operation, as modified by Polak. In the streptococic form of infection in which the patient has survived the acute stage, but where symptoms remain, operation is delayed as long as possible, as latent organisms are sometimes aroused to activity by operative interference, and an apparently simple case will die of streptococic peritonitis. In the high amputation operation, menstruation can be preserved and still the pathology can be removed. In doing this operation, one might ask why we should preserve the menstrual function. Although its preservation is considered purely sentimental by some, it seems worth while in those cases where it can safely be done. We must, however, remove all pathology irrespective of age or other conditions.

Lethal Dose of Roentgen Rays in Cancer.—Within the last few years, and especially since the introduction of the Coolidge tube, much has been accomplished in the establishment of suitable dosage for the therapy of superficial and benign skin lesions with the roentgen ray. The lethal dose for cancer cells, however, has not been accurately determined for filtered rays of short wave length such as are now used for deep therapy. For this reason some experimental work that has been performed by WOOD and PRIME (*Jour. Am. Med. Assn.*, 1920, lxxiv, 308) under the George Crocker Special Research Fund, is timely and of definite practical value. They found that approximately four erythema doses of roentgen ray, given continuously and filtered through 3 mm. of aluminum, are required to kill mouse carcinoma, and five to kill mouse sarcoma exposed *in vitro*; but occasionally some cells may escape the effects of even six doses. Approximately six erythema doses of roentgen ray are required to kill sarcoma cells *in vivo*, as compared to five required to kill the same cells *in vitro*; and approximately six erythema doses are required to kill carcinoma cells *in vivo* as compared to four to kill the same cells *in vitro*. The *in vitro* outgrowth from sarcoma tissue after four erythema doses of roentgen ray, still produced tumors when inoculated into mice and therefore the amount of *in vitro* growth is no indication whether the tumor cell is or is not capable of proliferating in the animal body. The growth observed after lethal doses is evidently due to the slow action of the rays, which permits cells potentially dead to wander out into the medium and to complete a division process before their growth momentum is finally checked. It is important to remember that absence of mitotic figures after roentgen-ray treatment is not an indication of lack of ability of the cells to grow in the animal body. The practical conclusion which may be drawn from these observations is that the amount of roentgen ray necessary to kill all the cells of a rapidly growing, very cellular and highly malign-

nant sarcoma or carcinoma in man is between five and seven erythema doses of filtered roentgen ray when the tumor is on the surface of the body. Every centimeter of tissue that covers the tumor makes an additional amount of roentgen ray necessary. For example, when slices of fibroid tumor are used as absorptive material the galvanometer deflections show that at a depth of 2 cm. 19 per cent. more roentgen ray is required; at 5 cm. depth, 47 per cent. more; at 10 cm. depth, 65 per cent. more. While many tumor cells may possibly be slowed in their progress and mitotic forms killed at such depths, it is doubtful whether all can be destroyed. The basal-cell tumors and the lymphosarcomata are, as is well known, much more susceptible to radiation. Small, superficial, metastatic carcinomata are also, in some instances, more susceptible than is the primary tumor.

OPHTHALMOLOGY

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Keratitis Profunda or Disciformis.—VERHOEFF (*Arch. Ophthalm.*, September, 1919, p. 449), in reporting an instance of this affection with microscopic examination, concludes that disciform keratitis may be produced by a variety of causes, and from an etiological standpoint is therefore not an entity. Certain cases are of the same nature as keratitis profunda. The corneal changes in the latter affection are due to the action of diffusible toxic substances arising near the anterior surface. The changes consist in alteration of the epithelium, destruction of the corneal corpuscles and injury to the stroma in the anterior layers of the cornea, and proliferation of the corneal corpuscle behind and around the injured area. In addition, there is injury to, or destruction of the endothelium, and in severe cases, deposition of fibrin and leukocytes on Descemet's membrane, behind the affected area. Leukocytic infiltration of the corneal stroma is conspicuously absent. The microscopic findings in the case reported strongly indicate a neuropathic origin for keratitis profunda.

Loss of Vision of One Eye Without Appreciable Organic Lesions Consecutive to a Shell Wound of the Other Eye.—LAPERSONNE (*Arch. d'ophthal.*, xxxvi, 639) reports the case of a soldier, aged forty-five years, who was wounded by a shell in the left eye with consecutive cataract and loss of vision of this eye. Subsequently the right eye developed marked functional disturbances, not due to sympathetic ophthalmia. Complete blindness supervened. Two years later, no lesion of the fun-

thus could be demonstrated; the pupil reacted normally; there is present depression of the visual line accompanied by immobility of convergence of both eyes. Morax and Souques also examined the case; they agreed in the diagnosis of blindness without appreciable organic lesion. The question of simulation was considered; but the patient under strict surveillance at the Hôtel-Dieu for eighteen days, constantly maintained the eye in the position noted. In spite of some doubt, the reporter recommended full pension for complete blindness of both eyes.

Gunn's Syndrome: Associated Movements of the Upper Lid with those of the Jaw.—AMAT (*Annal. d'ocul.*, September, 1919, p. 513) concludes that the syndrome is suggested physiologically in some healthy persons who open their mouths simultaneously with their eyes. Normally the superior branch of the motor oculi contains fibers derived from the motor portion of the trigeminus, indicating a functional synergy. In animals which keep the palpebral commissure open while eating, there must be anastomoses to assure such synergy. Although the functions of these fibers in man are unimportant or rudimentary, it may happen that in ptosis of the lids, their power develops and even surpasses the normal limits, constituting an additional function rather than a synergy. The junction of these fibers from the fifth nerve with the third must take place at the periphery; there must also be peripheral liason between the fifth and seventh, third and fourth, third and sixth cranial nerves and between the latter and the sympathetic. The superior branch of the motor oculi frequently receives, in the orbit, a filament from the ophthalmic nerve or its nasal branch; although this may contain, as is probable, no motor fibers, it strongly suggests the possibility of other anastomoses, motor in this case, between the trigeminal and third nerves. The above hypothesis explains (1) cases in which the syndrome is present without ptosis, both congenital and acquired; (2) its coincidence with palsies of the levator whether of cortical, subcortical, nuclear or funicular origin (the third nerve contains no filaments from the motor portion of the trigeminal which reach it in the orbit or its neighborhood); (3) the cure sometimes is obtained by training isolated movements of the lids by the will and thus frees the connection which unites the movements of the latter to those of mastication.

Traumatic Cataract after War Injuries.—POULARD (*Annal. d'ocul.*, October, 1919, p. 621) reports 55 cases all submitted to late operations. Thirty-eight followed wounds of the eye, the remainder contusions; the results were least favorable in the first class. In 4 cases the vision was nil or nearly so; in 13 from $\frac{1}{50}$ to $\frac{1}{20}$; in 13 from $\frac{1}{10}$ to $\frac{1}{5}$; in 24 from $\frac{1}{4}$ to 1. Their unsatisfactory results as regards visual acuity were dependent upon lesions of the fundus.

Papillary Stasis and Dilatation of the Ventricles in Cerebral Tumor.—Papillary stasis may be caused by lesions of very diverse natures and seat, but whatever the lesion, the stasis is always the result of intracranial hypertension, of which in fact, it is the capital symptom. Based upon anatomico-clinical studies of 27 cases, for the most part unpublished, BOLLACK (*Paris Thesis*, 1919, *Arch. d'ophtal.*, September-October,

1919, p. 701) has shown the constant occurrence of dilatation of the third ventricle in papillary stasis. Tumors of the posterior region are almost constantly accompanied by dilatation of the ventricles, either localized in the third or present in all. In tumors of the convexity, the dilatation is not constantly present; when it is, it is localized in the third ventricle. The latter, accordingly, appears to play an important role in the apparition of papillary stasis; distention of one or both lateral ventricles is only accompanied by papillary stasis when the third ventricle is also dilated. Dilatation of the lateral ventricles takes place through the foramina of Munro. Dilatation of the ventricles in the course of cerebral tumors is consequent upon perturbations in the secretion, absorption and especially drainage of the cephalorachidian fluid from the ventricular cavities to the subarachnoid space; hypertension, then dilatation of the ventricles. Papillary stasis is well-nigh constant in ependymitis and serous meningitis, so-called internal hydrocephalus; in these cases there is also ventricular distention. On the other hand in affections which but rarely cause distention, such as cranial traumatism, tuberculous, syphilitic or cerebrospinal meningitis, papillary stasis is inconstant. Certain other systems found in cerebral tumors bespeak the occurrence of hypertension of the ventricular fluid and the distention which results therefrom, such as hypophyseal syndromes and alterations of the sella turcica as shown by radiography; moreover, it is sometimes possible to discover differences of tension between the ventricular and cephalorachidian fluids. The writer has attempted to supplement his researches by experiments on monkeys, but he was unable to provoke either papillary stasis or ventricular hydrocephalus. He concludes that dilatation of the ventricles explains the pathogenesis of papillary stasis either indirectly or by the direct action of the ventricular hypertension upon the chiasm. This hypothesis, based upon the intimate embryological, anatomical and histological connections between the third ventricle and the chiasm, seems, moreover, justified by the presence, in papillary stasis, with ventricular dilatation of microscopic lesions in the chiasm.

Ocular Functions of Aviators.—WILMER (*Arch. Ophthalm.*, September, 1919, p. 439) in a paper upon this subject, insists upon the necessity of absolute normality of the eyes. Affections of only passing inconvenience on the ground, such as scintillating scotoma, muscae volitantes, photophobia, heterophoria and for the night flier poor dark-adaptation, are serious in the air. A successful combat pilot, with trained air vision who loses one eye, may be returned to flying status, but only when confidence is unimpaired and there is eagerness to get back. Regular eye re-examinations should be made every two months at least. The simple visual reaction time is of great value if associated with cool determination and caution.

Primary Sarcoma of the Iris.—Primary sarcoma of the iris is an exceedingly rare growth. DeWecker, with his large experience, states that he never saw a case. Fuchs in an analysis of 259 cases of sarcoma of the uveal tract found but 16 which began in the iris. Lawford and Collins note but one primary growth of the iris in 103 cases of uveal sarcomata. FAGE (*Arch. d'ophthal.*, xxxvi, 678) reports a case of leuko-

sarcoma, a tumor even rarer than melanotic sarcoma, so that Lagrange was able to find but 8 cases in the entire literature of ophthalmology. The case reported by the author is further remarkable for rapidity of growth; in less than a year a glaucomatous attack was set up and enucleation was necessary. Generally, sarcomata of the iris develop slowly; periods of from twelve to twenty-five years have been reported. Simple excision of the tumor has given satisfactory results in some cases, but this method is uncertain. Enucleation is generally to be preferred, and in all cases in which glaucomatous attack has supervened, or there is rapid growth, or the surrounding parts invaded.

School Myopia and Emmetropization.—DINGO (*Amsterdam Thesis, Arch. d'ophtal.*, xxxvi, 700) remarks that the etiology of school myopia has not yet been sufficiently cleared up, neither by the theory of accommodation nor by that of convergence. The writer has studied the influence of the position of the pupil upon the configuration of the eye when the upright attitude is maintained with the head and body inclined forward; by means of comparative photographs the eye is pushed forward to a considerable extent in the latter position, involving traction of the globe upon the optic nerve, which will be followed by lengthening of the anteroposterior diameter of the eyeball, which involves the development of myopia.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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PITTSBURGH, PA.

Studies on Endothelial Reactions: The Macrophages of the Loose Connective Tissue.—Within the last twenty years, many studies of the large phagocytic mononuclear wandering cells of the body have appeared in the literature. Even more numerous have been the discussions of intravital stains and the methods and results of their use. A number of workers have employed either the benzidine dyes in colloidal solution or various finely divided inert substances in suspension in an attempt to determine the origin of the large phagocytic mononuclear wandering cells which appear with some slight modifications of form in many sites throughout the body. Recently, FOOT (*Jour. Med. Res.*, 1919, xl, 353) has brought forward an ingenious combination of the two types of intravital stains, in an attempt to trace to its source the large mononuclear wandering phagocytic cell of the loose connective tissues. To test out the older work, in which it was claimed that the large phagocytic mononuclears were of omental or of connective-tissue origin, trypan blue was injected intraperitoneally. The administration of lampblack intravenously was carried on at the same time, in order to mark the cells should they prove to be of endothelial origin. The

subcutaneous and intramuscular connective tissues were injected with sterile agar, to serve as a foreign body around which the large mononuclear wandering cells might congregate. A rabbit was saturated with trypan blue by the peritoneal route, injections of this dye given almost daily, while at the same time an emulsion of 5 per cent. lampblack and 1 per cent. gelatin in normal salt solution was given in small doses into an ear vein. During the staining process, sterile agar was injected daily under the skin of the back over a period of thirteen days, and a series of intramuscular injections was likewise made. At the termination of the period noted, the lesions were recovered and fixed in formalin, and blood smears were made and stained by Wright's method. The gross appearance of the tissues at autopsy showed evidence of thorough vital staining, the spleen, and rather remarkably, the lungs, being described as of a sooty, brownish blue color. The blood smears showed a normal cell count for the rabbit, and it is to be particularly noted that of the cells listed as endothelial leukocytes, 70 per cent. showed carbon granules. Rarely, these cells were loaded with carbon, but usually there were only two or three granules. In regard to the fate of the carbon, microscopical examination indicated that the endothelium of capillaries, lymphatics and even medium-sized vessels had taken up moderate amounts of the material. The omentum showed extensive staining with trypan blue, making the endothelial cells difficult to distinguish from the mesothelial cells; but there was more carbon in the region of the vessels than elsewhere, and occasional isolated mononuclears with carbon pigment were considered as endothelial cells which had migrated with their load of carbon. The lungs, spleen and liver were the organs in which the bulk of the lampblack was taken up by the endothelial cells. The author notes that the heavy toll on the circulating carbon granules by the endothelial cells of the organs mentioned greatly decreases the supply available to possible proliferating and vitally staining cells in the local reactions about the injected agar. The reactions about the agar mass, as presented in the series of lesions at different time periods revealed a number of interesting points. These may be briefly summarized. After twenty-four hours, the vessels in the region of the agar, showed proliferation and increase in the size of the lining cells, a number of which also contained carbon granules. There were similar cells containing only carbon granules, free in the tissues about these vessels. These became fewer as the distance from the vessel was increased, and about 30 per cent. of them showed granules of carbon. Clasmatocytes showing trypan blue and carbon granules were scattered sparsely in the connective tissues. As the lesions at increasing time periods were examined, it was possible to trace the development of migrated mononuclears from the bloodvessels through a stage exactly resembling the clasmatocytes and finally to their clumping together as syncytia about the agar mass. The percentage containing carbon continued as on the first day. Mitoses in the clustered cells were noted, and as the syncytia developed, the carbon granules became more scattered in the cytoplasm. A faint trypan blue stain appeared in the syncytial cell groups, in the older lesions. By the seventh day, the migration of endothelial cells had ceased. In the intramuscular injections, it was found that the small granular mononuclear cell normally found in the stroma of muscle had proliferated and had taken an intense trypan blue stain, as well as

carbon granules. As the vascular endothelium, with the exception of that of the sinuses of the liver and spleen, did not take trypan blue the author is at a loss to definitely identify this group of cells. As he noted the same reaction in the endothelial cells in the region of the panniculus carnosus in the subcutaneous series, he offers the suggestion that muscular metabolism may be a factor. From the foregoing, Foot concludes (1) that the macrophages of the connective-tissue spaces are of endothelial origin, (2) they are not derived from the omentum nor (3) from lymphocytes; and (4) that a few seem to be of doubtful origin, notably the small granular cells of the intermuscular connective tissue.

Bacteriological Analysis of Fecal Flora in Children.—In support of the clinical observation that the presence of a putrefactive flora is associated with a certain syndrome, importance being given to the recognition of various types of fecal flora, such knowledge assisting in the dietary management of cases, MORRIS, PORTER and MEYER (*Jour. Infect. Dis.*, 1919, xxv, 349) present an extensive bacteriological analysis of feces in normal and sick children. Details are given of the technic of collection of material and methods of examination. Gelatin, Loeffler's serum, cresol purple milk, lactose peptone bile, endos and various other carbohydrate media were used, following a differential count of organisms in direct smear stained by Gram's method. The differential count alone, of bacteria in direct smear is considered of little value. Three types of intestinal flora were delineated: fermentative or saccharolytic, normal or facultative and putrefactive or proteolytic, each group consisting of bacteria of rather distinctive characteristics. Cultural findings in infant stools vary from those in adults. Interesting variations were shown on different carbohydrate media in fermentation tubes. Putrefactive flora consisted principally of *Bacillus coli*, Gram positive spore bearing rods and streptococci, with few aciduric organisms. In a fermentation flora aciduric organisms predominated, very few *Bacillus coli* being present. Transformation of fecal flora from putrefactive to fermentation was shown by liberal carbohydrate feeding, *Bacillus acidophilus* and *Bacillus bifidus*, being the organisms whose establishment in the intestinal tract, bringing about the change in stool. Feeding of *Bacillus acidophilus* was also successfully undertaken to bring about this change. In either case, usually by combination of both methods, the change in type of flora takes place in two to six weeks, and is permanent only when animal proteins are excluded from diet and rich carbohydrate feedings are given. Maltose, lactose, and dextrose were found to be the substances most suitable for control of proteolytic organisms of the digestive tube.

Epidemic of Water-borne Dysentery.—An epidemic of bacillary dysentery, Flexner type, occurring among the inhabitants of Bertrichamp, France, is reported by STOOKEY (*Jour. Infect. Dis.*, 1919, xxv, 331), in which the source of the infecting agent was found to be a latrine, which drained downward to a point in the town water supply line, about fifteen feet away, where there was found a broken joint. All patients had practically identical symptoms and admitted having drunk water from the public supply about two or three days before the onset of their illness. Mortality in the epidemic was 33 per cent.

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.

Mortality Statistics of Wage Earners and their Families.—DUBLIN and KOPF in a recent book published by the Metropolitan Life Insurance Company, under the title "Mortality Statistics of Insured Wage Earners and Their Families" touches a field which, up to this time, has received too little attention from those interested in preventive medicine and public health. Since 1900, there have been available the annual mortality reports of the United States Census Bureau. These relate to the general population. The volume just published by the insurance company, however, relates to the mortality of its industrial policy-holders. This means that the death-rates are those of wage-earners and their families residing almost entirely in urban communities. No such data are available from any other source. Since the compilation is made along the same basic lines as those by the Census Bureau, public health and social workers, sanitarians and others have now, for the first time, an opportunity to compare health conditions in the general population with those of the wage-earning group. Six years (1911 to 1916 inclusive) are covered in this book. During that period, there were more than 635,000 deaths, and about fifty million years of life are represented. The significance of this is that with the immense number of lives at risk, in almost all of the States of the Country and the provinces of Canada, there is certainty that the figures are representative figures. A large number of tables appear showing deaths and death-rates by color, sex and age for all of the more important diseases and conditions. Others show the trend of the mortality for each important cause of death throughout the six-year period. It is shown that for all age groups under twenty-five years, there is no marked divergence in the mortality of wage earners and of the general population. After age twenty-five, the mortality of male wage earners is markedly in excess of that for males of corresponding ages of the general population. With females, the experience is very similar, although the excesses in the wage-earning groups do not begin to manifest themselves until the age of thirty-five is reached. Various factors are responsible for the higher death-rates of the industrial group. Among them, may be noted the comparatively larger number engaged in arduous labor and hazardous occupations, the care of larger families with smaller incomes, together with lower standards of diet, housing, clothing and medical service. Then too, there is the very important fact that the Industrial policy holders constitute practically an urban group, whereas only

one-half of the general population live in the cities. The death-rate of the colored policy holders is over 50 per cent. in excess of the whites. This condition obtains for both males and females. In some age groups and for certain causes of death, the situation is even more unfavorable. Thus, for tuberculosis of the lungs, colored males under age fifteen showed death-rates about ten times as high as white males at the same ages and, colored females, between eight and nine times as high as white females. The more important diseases are discussed in special chapters. Notable among these are tuberculosis, organic diseases of the heart, pneumonia, Bright's disease, cancer and others. For each disease, interesting and valuable comparisons are made showing the differences in the mortality experience of the general population and the wage earners. Among the diseases in which a marked downward trend in mortality was observed, are typhoid fever, scarlet fever, diphtheria and tuberculosis. The mortality from diabetes showed a tendency to increase. There were no important changes in the death-rate among the industrial classes for cancer, organic heart diseases, cerebral hemorrhage, Bright's disease, causes incidental to pregnancy and childbirth, suicides and accidental deaths. Qualified workers may obtain this volume by writing to the Company.

Pollution of Certain Tidal Waters of New Jersey, New York, and Delaware, with Special Reference to Bathing Beaches and Shell-fish Bearing Areas.—CUMMING'S (*Public Health Bulletin No. 86*, U. S. Public Health Service, August, 1919) studies cover a large amount of field and laboratory work in some of the most populous and important coastal areas in the United States. The chief points in his summary are as follows: As a result of the laboratory examination and sanitary surveys made by the service, it has been determined that the waters in which these shellfish are grown are, with the exception of the small areas described, free from pollution. However, almost all of the oysters grown in these waters are removed to small creeks or rivers, where the salinity of the water is less, for the purpose of "floating" or "freshening" before shipment. The sanitary condition of such oysters depends upon the condition of these creeks rather than that of the beds on which they are grown, and some of these "drinking" places have been found to be unsatisfactory. Throughout the State the New Jersey Department of Health has been found to have been active in attempting to remedy dangerous conditions wherever they exist, and it is believed that this organization as at present constituted will do even more efficient work in the future. In addition to the great value of the coastal waters of New Jersey in connection with the shellfish industry, these waters are of far greater value because of the number of summer resorts along the whole shore from Sandy Hook to Cape May. The protection of these waters from pollution and nuisance is therefore of the utmost importance to the State, and because shellfish are shipped from the State throughout the country, and the resorts are visited annually by hundreds of thousands of citizens of other States, the sanitary conditions of the resorts and of the coastal waters is a matter of national moment. People who go to such resorts are gradually being educated by the various public health agencies as to the possible danger of contracting diseases in insanitary surroundings, and are beginning to consider the health-

fulness of a resort as an important factor in determining where they shall spend their vacation. As a result the citizens of the resorts are beginning to realize the monetary value of good sanitary measures, and there seems to be a general appreciation of the necessity for maintaining good sanitary conditions in the communities along the coast. One source of considerable danger exists nearly everywhere along the inland waterways in the vicinity of communities or cottages with sewerage systems. Bulstrode and others have called attention to this danger in England. It seems to be a common custom for cottagers, boarders, and "trippers" to dig clams, for pleasure or profit, without reference to the proximity of sewer outfalls. Indeed, such places often seem on account of their convenient location to be favorite localities with such people. This problem would appear to be one for local sanitary police regulation, although it is of general interest because of the fact that these people come from all sections of the country. The use of large warning posters such as are displayed near Atlantic City is to be commended.

Deer-fly Fever, or Pahvant Valley Plague.—FRANCIS (*Public Health Reports*, 1919, xxxiv, 2061) reports the occurrence in Utah of a disease characterized by septic fever and enlargement of regional lymph glands. The disease is popularly believed to be due to the bite of the deer-fly. Suitable animal experiments demonstrated that the disease is due to *B. tularensis*, which has been found to be the cause of a plague-like disease of rodents.

Pitfalls in Determining the Prophylactic or Curative Value of Bacterial Vaccines.—McCoy (*Public Health Reports*, 1919, xxxiv, 1193) calls attention to the difficulties attending the determination of the value of prophylactic agents in influenza. The commonest error is made by beginning the vaccinations after the disease has appeared in a group of persons. Those who developed the disease prior to the vaccinations are carried in the control group, while the vaccinated are the relatively immune part of the population, many of whom would not develop the disease in any event. A second source of error lies in crediting to the vaccinations the absence of the disease in a group all of whose members have been vaccinated, while in reality the protection may be due to quarantine or other circumstances. Finally, warning is given of the danger of drawing conclusions from meager data. It is insisted that only a portion of any group should be vaccinated, the remainder, comparable as to age, sex and conditions of exposure, being regarded as controls. It is pointed out that an efficient agent might fail because time has not been allowed for the immunity to develop.

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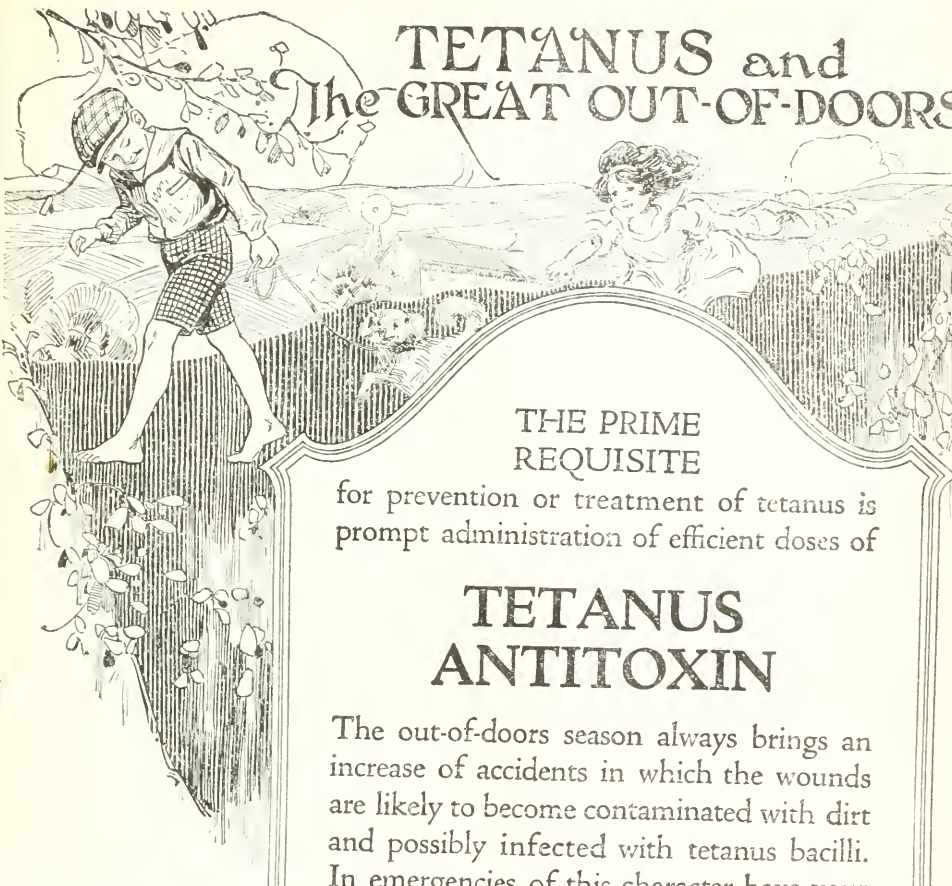
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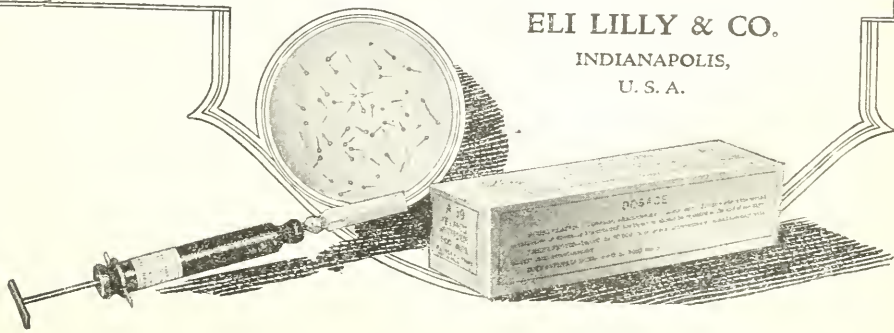
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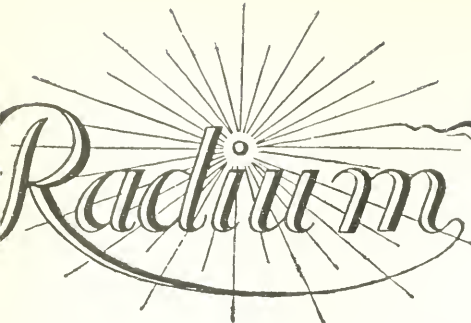
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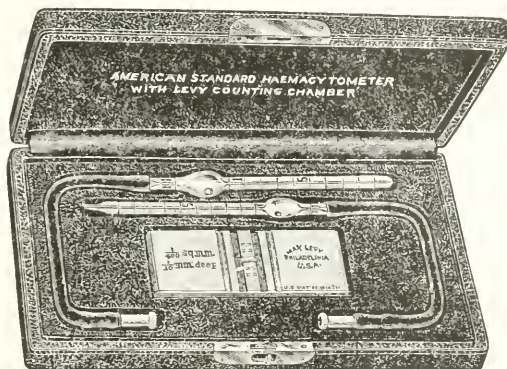
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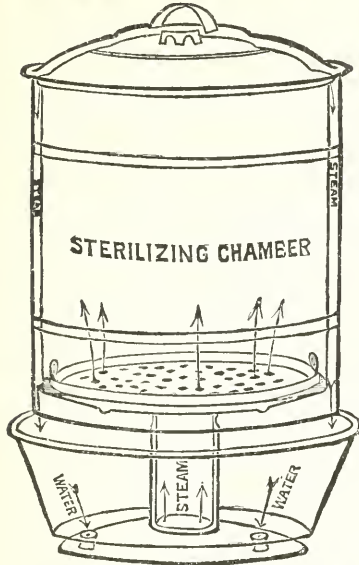
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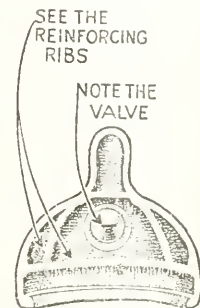
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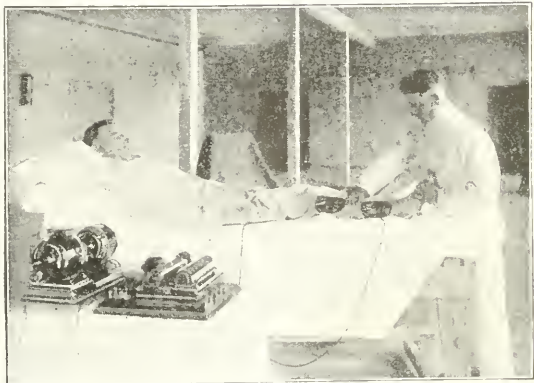
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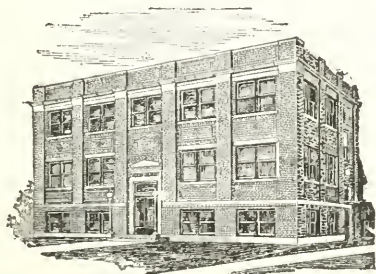
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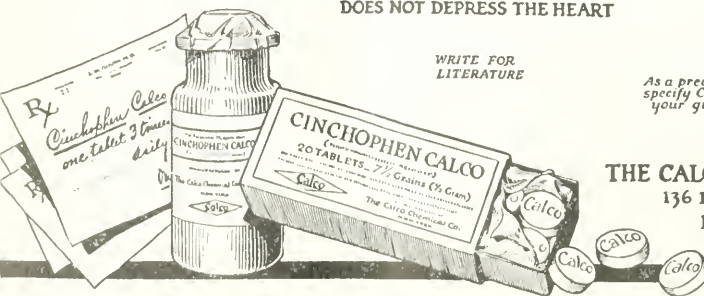
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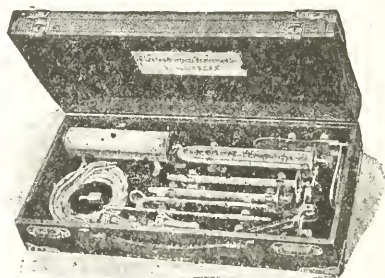
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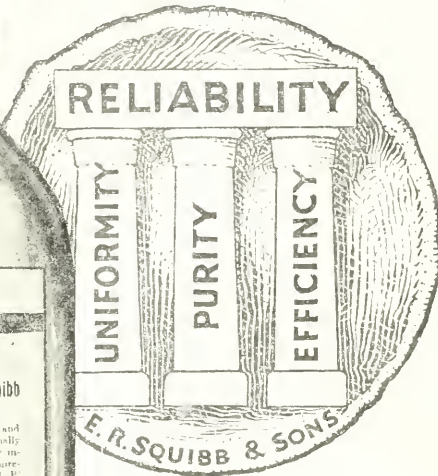
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JUNE, 1920

ORIGINAL ARTICLES.

CAUSES AND DEFINITION OF CANCER.

BY LEO LOEB, M.D.,
ST. LOUIS, MO.

(From the Department of Comparative Pathology, Washington University Medical School of Medicine, St. Louis, Mo.)

IN the present article we wish to summarize as briefly as possible our knowledge of the causes of cancer as far as our information in this field permits us to do so at present without exceeding the range of probabilities. The following factors may enter as causes of cancer:

- (a) External stimulation of a mechanical or chemical nature.
- (b) Internal chemical stimulation, especially through the action of internal secretion.
- (c) Heredity, which includes various not yet well-defined factors, some of them probably identical with the other "causes."
- (d) Embryonal character of tissue or disturbances of embryonal development; this includes parthenogenetic development of the ovum.

- (e) In an indirect way age may enter as a factor.
- (f) Contact between normal and cancerous tissue.
- (g) A possible effect of microorganisms.
- (a) *External Stimulation.* Observation of cancer in man has abundantly proved the significance of long-continued irritation or in some cases apparently even of a single trauma in the origin of

cancer. The same factor may play a part in cancer of animals. We have, for instance, shown that in this country the favorite seat of cancer in cattle is the inner canthus of the eye, where foreign bodies are liable to lodge and to cause irritation.

A number of investigators have attempted in a similar manner to produce cancer experimentally. The earlier experiments did not succeed, probably because the irritation was not applied over a sufficiently long period of time. (Hanau, Brosch.)

More recently similar attempts have been successful (Pierre Marie, Raulot-Lapointe and Clunet, Fibiger, Yamagiwa and Ichikawa). Through the application of roentgen rays two sarcomata have been produced at the root of the tail of rats, and carcinomata, some of which were metastasizing and transplantable, have been produced in the stomach and tongue of rats and in the stomach of mice after feeding with nematodes which settled in the stratified epithelium and stimulated it. Through the feeding of mechanically irritating material a cancer of the tongue has been produced in a rat. Following the application of tar carcinomata developed in the skin of the ear of rabbits. While those experiments are essentially a confirmation of what observation has shown to take place in nature, they are of the greatest significance, not because they establish a hitherto unknown cause of cancer but because they open up a new field for the experimental analysis of the conditions under which this cause acts and because they offer a chance for its quantitative analysis.

In a tentative way we may draw certain conclusions on the basis of these investigations.

1. There seems to exist a graded series of transitions from the normal growth energy and cell motility to the increased growth energy and motility of cancer. On the whole, the first stages seem to be similar in different kinds of cancers (similarity in the first stages of the experimental cancer of stomach, tongue, skin).

2. The increase in growth energy and mobility and in the length of time over which this increase persists after the stimulus has ceased to act appears to be gradual. Various intermediate stages seem to exist.

3. It is probable that in the experimental cancers produced by Yamagiwa and Ichikawa, and perhaps even in those of Fibiger the last stage, which we find in many spontaneous cancers of the rat and mouse and of man, had not yet been reached. Thus the experimental cancers in the ear of rabbits retrogress in a much greater proportion of cases than do spontaneous cancers. The most virulent case of cancer in the stomach of mice died out after a few transplantations.

Transplantability as such is not necessarily a characteristic of cancerous tissue. Many spontaneous cancers cannot be transplanted successfully. And, on the other hand, we did accomplish

a serial transplantation of a benign tumor in a rat. It likewise died out after a few transplantations. Even normal tissue can be transplanted repeatedly. But each kind of tissue maintains, on the whole, the growth energy characteristic of it, and this is one of the essential distinguishing features between cancer, benign tumor and normal tissue. Besides cancer tissue, proliferating very actively, may escape the action of homoiotoxins much more effectively than normal tissue. Whether the early dying out of Fibiger's tumor was due to accident or to a gradual weakening of the growth energy or to a combination of both these factors, cannot be stated by us with certainty. It is probable that in this case the increase in growth energy had persisted over a considerable period following cessation of the stimulus; but that the increase had not yet become permanent.

This conclusion seems to apply with much greater definiteness in the case of the experimental cancers in the rabbit ear. The tissues used in these experiments are evidently relatively resistant to the cancerous transformation, as evidenced by the fact that spontaneous cancers have not been observed in the ear of the rabbit and are very rare in the stomach of rats or mice.

4. While it is thus very probable that the transition from normal to cancerous tissues represents a series of stages, the transition from one stage to another may be abrupt. The cancerous tissue may differ sharply from the precancerous tissue morphologically and biologically. It is, however, possible that a continuous not visible change precedes this abrupt transition. It is probable that also in man certain cancers have not yet reached the last stage of cancerous transformation. In certain cases their actual and potential proliferating power seems to be as yet relatively low and it is not improbable that in some cases these changes have not yet become permanent. At present the demarcation between those transitional stages which are and which are not yet cancerous is to some extent arbitrary.

5. We may furthermore conclude that the earlier the stages in the transformation leading to cancer the greater is the tendency to retrogression in the cancerous transformation which can be produced experimentally, and that the earlier stages yield more readily to the action of agencies which tend to destroy them.

(b) *Internal Secretion.* Three sets of experiments might be cited as disproving the significance of internal secretion as one of the causes of cancer: (1) The lack of success in the attempt of surgeons to cure cancer of the mammary gland through castration. (2) The fact that in castrated cattle and horses cancer is, on the whole, as frequent as in not-castrated animals. (3) The fact that in castrated mice inoculated tumors grow in a manner not very different from that observed in normal control mice. Yet none of these facts disprove the significance of internal secretion in the development of cancer. The first observation is in all probability to be attributed to the fact that internal secretion has no definite influence on the

growth of cancers after they have once developed. The negative result in the second observation is due to the fact that the relation between internal secretion and the development of cancer is not a general but a specific one. Castration cannot influence the origin of cancers in organs in which the growth processes are not normally directly dependent upon the internal secretion of the ovary. The third observation which relates to the condition under which inoculated tumors, "homoiotumors," cancers which are already well established, grow, can have no bearing on the problem of the origin of tumors. In two series of experiments we could indeed show quite definitely that castration has a definite influence on the origin of mammary cancer, which is the usual cancer in mice. Not only can it be proved that a hormone given off by the ovary regulates those tissue changes which lead to the development of cancer of the breast in mice, but it can, furthermore, be shown that the influence of this hormone is a quantitatively graded one. If the quantity of this hormone, which had a chance to act on the tissues, exceeds a certain limit, cancer appears as frequently as in non-castrated controls (castration at the age of eight to ten and one-half months); if an intermediate quantity of the hormone has been active the cancer rate is noticeably diminished and the cancer seems to appear later in life (castration at the age of five to seven months); if the quantity of the hormone is still further restricted cancer does not appear at all or only exceptionally (castration at the age of three $\frac{1}{2}$ to five months). After an intermediate and late castration tumors may not only appear in the first-age period, but even tumors which in control mice appear as late as the third-age period are not prevented from developing. This suggests the conclusion that the first tissue changes which eventuate in the development of cancer occur at a much earlier period in life than might have been expected, and that castration affects these primary tissue changes rather than the secondary transformation of these changes into fully developed cancer.

Experimental investigations have made possible in this case a quantitative analysis of a definite cause of cancer, and it will now probably be possible to analyze experimentally in an exact manner the conditions underlying the origin of cancer of the breast in mice. The effect of hormones on the development of cancer is a specific one; a hormone influences the development of cancer only in those organs to which under normal conditions it has a specific relation. We may assume that relations similar to that between cancer of the breast and the ovary exist also between the development of other kinds of cancer and the organs with which they are related through internal secretion. It follows from our experiments that attempts to cure cancer of the breast after it has once been established cannot be successful. Our experiments have established, furthermore, the fact that nursing and the injuries due to it or pregnancy

in general have only a negligible influence on the frequency with which mammary cancer develops in mice.

(c) *Heredity.* It is commonly assumed that heredity plays no part in the origin of cancer in man, and as late as 1910 Bashford expressed the opinion that heredity has no significance in the etiology of cancer in general. The prevalence of this view is due to the fact that the methods used were those usually applied in human mortality statistics; the frequency with which cases of cancer occur in the ancestry of persons dying from cancer and other diseases was compared. No noteworthy differences could thus be found in man at least among the white races. Tyzzer and Murray approached the same problem in the case of mice with somewhat similar methods. Murray compared the frequency of cancer in these animals among those individuals whose mother or grandmother had cancer, on the one hand, and among those in whom cancer had not been observed in the direct ancestry but may have occurred in the great grandparents. Murray found on the average about 20 per cent. of cancerous mice among those whose direct ancestors had suffered from cancer and 11 per cent. among those whose direct ancestry had been free from cancer. In certain age classes the cancer rate of both kinds of mice showed only a very slight difference, and in one age class the cancer rate was even higher in those whose direct ancestry had not been affected by cancer. Nevertheless the figures of Murray point to the conclusion that heredity plays a part in cancer of mice. There are, however, certain difficulties implied in the method used by this author. A certain mouse may be cancerous and still the hereditary tendency in the family of such a mouse may be much less strong than in another mouse which did not die from cancer. This method can therefore at best only make probable the existence of a hereditary factor in the origin of cancer in mice. It cannot give definite knowledge of the significance of heredity, and in particular it cannot give an insight into the quantitative factors which are concerned in heredity. In order to determine to what extent the hereditary tendency to cancer varies in different families, whether the hereditary tendency to cancer in a certain strain is a constant or may become modified under certain conditions, and what the laws of heredity are in hybrids between strains rich and poor in tumors, we have to use a different method and try to follow the fate of separate families or strains of families through successive generations. Earlier observations on the so-called endemic occurrence of cancer in cattle and rats suggested to us the possibility that heredity might be responsible for this condition. But it was only about twelve or thirteen years ago that we began with Miss Lathrop to make observations on the difference in hereditary predisposition to cancer in the different strains of mice which were raised in her breeding establishment. Preliminary observations indicated differences in the cancer rate in different

strains. Since 1910 we have kept systematic records of the cancer incidence in the various strains on the cancer age and on the effect of hybridization on the cancer rate in the offspring.

In thus keeping families or strains of mice separate through successive generations we find that the cancer rate in different strains shows extreme differences. While in some families it may be as high as 70 to 80 per cent. or even higher, in others cancer may be very rare or absent. All intermediate degrees are found in other families. In some cases we could separate substrains differing sometimes but not always in color and other characteristics and which had a cancer rate different from that of the main strain. In this case we had in the beginning probably to deal with mixed material from which a more homogeneous line could be detached. In those strains in which the cancer rate is high an absolutely greater number of tumors appear usually in young animals than in those with a low tumor rate; but a certain difference exists in this respect in certain strains and within certain limits the cancer age seems to be a hereditary characteristic at least in the case of some families. Thus a number of strains may have a similar cancer rate, but in some of them many cancers appear in relatively young animals, while in other strains the great majority of cancers appear in older mice.

If we follow such strains through a considerable number of successive generations we find in many of them a surprising constancy in the cancer incidence. In some cases, however, changes occur which can in all probability be referred to one of these two conditions: (1) A selective action takes place as the result of which certain substrains with a somewhat different hereditary tendency to cancer become predominant in number, usually as the result of a more or less accidental condition, or (2) as the result of long-continued inbreeding not accompanied by selection of the strongest individuals the character of the strain changes in certain respects, and these changes entail corresponding changes in the cancer rate. A lowered vitality and breeding activity were accompanied by a lowering in the cancer rate.

If we hybridize different strains or substrains the cancer rate of the offspring is as follows: (1) In cases in which the cancer rate and cancer age of both parent strains are similar the cancer rate and age of the hybrids correspond to that of the parents. (2) If the cancer rate and age of the two parents differ very much the cancer rate of the offspring is often intermediate; there occur, however, all transitions from an intermediate condition to various degrees of dominance of one of the parents over the other. The parent with the higher tumor rate was, however, dominant in a considerably larger number of cases than the parent with the lower tumor rate in the strains with which we carried out our experiments. There is an indication that possibly in certain cases the mother

strain is of more importance in determining the cancer rate of the hybrid than the father strain, and that therefore one or more of the hereditary factors determining the development of cancer may be sex-linked. At present this is merely a suggestion, and further investigations must decide definitely whether or not such a relation exists.

From all these experiments we may, as we have pointed out previously, draw the conclusion that the hereditary tendency to cancer does not follow the laws of simple Mendelian inheritance of monohybrid characters; that it can, however, be explained according to Mendelian principles if we assume the presence of multiple hereditary factors. The inheritable tendency to cancer apparently does not consist in a tendency of the animal to develop cancer indiscriminately in any part of the body, but only in particular organs. Thus according to our observations mice with a very high incidence of mammary cancer do not usually develop cancer in any other organ but the breast. Miss Slye's discovery of families of mice with an inheritable tendency toward cancer in organs in which usually cancer occurs not at all or only very rarely is in agreement with this conclusion.

While it is now generally conceded that in the cancer of mice hereditary factors are of significance, it is, on the other hand, almost universally accepted that in human cancer hereditary factors do not play a part and that therefore a marked difference exists in this respect between these two kinds of cancer. However, it seems to us that a critical review of the evidence at hand does not justify such a conclusion; on the contrary, there is much evidence for the view that conditions are similar in both cases. The apparent difference is probably due to two factors: (1) In man the usual statistical methods are employed. Thus it is determined whether in the ancestry of persons affected by cancer the cancer incidence is considerably greater than in persons not thus affected. We have seen that even in the case of mice such statistical methods can at best give only a very inadequate view of the great differences caused by heredity in the cancer rate of different strains. (2) If we assume that in mice a constant interbreeding between diverse strains differing markedly in their cancer rate had taken place, there would undoubtedly after a certain period of time have occurred an equalization in the cancer rate of the various mixed families. Through statistical methods no or at best only a slight difference would have been detected in the ancestral cancer rate of individuals affected by cancer and those not thus affected. An occasional more noticeable difference encountered would probably have been explained as a chance occurrence. Yet while the interbreeding would to some extent have equalized the cancer rate in different families, it would therefore not have destroyed the hereditary factor of predisposition, but it would merely have distributed it quanti-

tatively in such a way that no marked differences could have been discovered between different families. Now this is what actually has taken place among the civilized races. Divergencies in the hereditary cancer rate which originally would perhaps have been quite noticeable might have been obscured through constant intermarriages. There is some evidence which seems to sustain such a conclusion. If we compare the cancer rate in human strains in which such intermarriages have not taken place, we find indications of a difference in the cancer incidence in these strains. Thus there can be little doubt that the aborigines in Africa and elsewhere differ in many cases markedly from the majority of the civilized people in their incidence of cancer and in the kinds of cancer from which they suffer. The negro in Africa and the pure Indian in this country may be cited as examples. Even among civilized people divergencies in the cancer rate seem to develop if the population is of a more sessile character and if distinct strains are formed through constant inbreeding and lack of intermarriages between different strains. At least this seems to hold good in certain parts of Norway according to the observations of Garmann. In America the cancer rate of the negro seems to be lower than that of the white race but higher than that of negro in Africa; this may be due to frequent intermarriages which have occurred between the two races. It is, however, possible that changes in the mode of living may also play some part in this result.

It is furthermore a well-established fact that various conditions which predispose to cancer are hereditary, such as pigmented nevi; the same holds good in the case of other hereditary abnormalities. Taking into consideration all these facts we may consider it probable that heredity is also a factor in the origin of human cancer, but that in the latter interbreeding and perhaps other factors have obscured this significance of heredity.

Such an interpretation may perhaps be of service in explaining, at least in part, the increase in the cancer rate which has been observed in all countries where statistical methods are employed. While it is still possible that this increase is only apparent, yet there is some evidence which makes at least probable the conclusion that an increase has actually occurred in most civilized countries. Now, if we assume that in human cancer the same conditions prevail which we found in cancer of mice, where in the case of our strains the higher cancer rate of one parent dominated over the lower cancer rate of the other in the majority of cases, such a slow increase in the cancer rate might be foreseen as the result of constant intermarriage. If intermarriage between individuals differing slightly in their hereditary tendency to cancer occurred constantly, it might lead to a gradual slow increase in the cancer rate, which would continue until at last the hereditary tendency has been almost equalized through constant interbreeding. Other conditions

such as changes in the mode of living which are taking place almost universally may perhaps be a contributing factor.

As to the character of the factors underlying the hereditary tendency to cancer our knowledge is not yet definite. We may, however, assume that in all probability different factors play a part. In some cases it depends apparently on differences in the readiness with which the transition from the earlier to the later stages of cancerous transformation are made by various tissues of the same individual and the same species. Differences in the amount of resistance which analogous tissues offer to acceleration in growth may be found normally. Thus we have observed that the mammary gland of the guinea-pig opposes a greater resistance to proliferative stimuli emanating from the ovary than the mammary gland of the rat or rabbit. On the other hand the epidermis of the guinea-pig possesses inherently a greater proliferative activity than the epidermis of the rat or pigeon. A quantitatively graded reduction in the amount of ovarian internal secretion still permits the development of mammary cancer in certain individuals but not in others.

In Fibiger's as well as in Yamagiwa's and Ichikawa's experiments the tendency of the tissues to take the first steps toward an increase in proliferative activity was widespread; in the later stages the tendency to acceleration in proliferative activity diminished and became restricted to a smaller number of individuals which were perhaps endowed with a greater lability of the tissues. In other cases the hereditary tendency consists in the hereditary transmission of cell groups which are especially liable to assume greater growth activity, as, for instance, pigmented nevi. Conversely the hereditary freedom from cancer may be due to a lack of tendency toward such diseases as predispose to cancer. Thus it is probable that the absence of gastric cancer in the Indian is in part due to his freedom from such gastric diseases as predispose to cancer. This hereditary variability in the liability of tissues to respond to proliferative stimuli may in certain cases perhaps be caused by variations in the amount of "sensitizing" substances which have the property of making tissues, which would otherwise have been inert, to an unusual degree responsive to various growth stimuli, which in themselves may have only a very restricted intensity. Thus we have shown that normally the corpus luteum substance sensitizes the tissues to the action of otherwise indifferent mechanical stimuli. Perhaps in different individuals the production of the ovarian hormone which stimulates the proliferative activity of the mammary gland differs in strength or quantity. These represent at the present problems which are not yet solved, but seem to be accessible to an experimental attack.

On the whole we may conclude that in all probability the character of hereditary factors is not different from other causes leading

to cancer. They seem to consist in the presence or absence of chemical or mechanical growth stimuli which originate within the organism, and which, while in themselves they are often not able to produce cancer, do so if combined with other growth-promoting factors. We must include in this category conditions which make tissues receptive, sensitize them to the action of mechanical or chemical growth stimuli. Such conditions may perhaps originate through a mutation localized in a chromosome. Thus Miss Stark has observed in the fly *Drosophila* a hereditary localized abnormality of growth which showed a certain resemblance to tumors in vertebrates. Boveri went so far as to explain changes in the chromosomes in the nuclei of somatic cells as the only cause of cancer, irritation and inflammation acting only indirectly in calling forth changes in the distribution of chromosomes which cause excessive tumor growth. While we must indeed assume that the hereditary factors in cancer are localized primarily in the chromosomes and that in those changes in proliferative and motor activity which constitute the cancerous transformation changes in the nucleus and particularly in the chromosomes may be involved, some experimental facts can hardly be reconciled with Boveri's generalization. I refer, for instance, to the gradations in cancerous transformation which have been shown to exist, to the quantitatively graded effect of internal secretion, to the contact-combination tumors, to the necessity of long-continued stimulation which is so noticeable a feature in the origin of most cancers as contrasted, with the readiness with which abnormalities in chromosome distribution can be brought about through single experimental interferences.

(d) *The embryonal character of tissue or disturbances of embryonal development and parthenogenetic development of ova* in the ovary play essentially a predisposing role in the origin of cancer. They provide a substratum which has a greater tendency to proliferate and is more receptive to abnormal growth stimuli which may reach it. We know that cancer which is once established grows better in young than in old individuals. The young tissues grow more actively than older tissues, and in addition the body fluids in younger organisms are more favorable to proliferating tissues than those of older individuals.

Embryonal tissues which begin to develop under abnormal conditions are thereby exposed to abnormal stimuli and thus may in certain cases be transformed into cancer. It is characteristic of many cancers whose origin is embryonal that their constitution is complex, they being usually composed of more than one kind of proliferating tissue. Especially in the germ glands, but also elsewhere, they may resemble malformed embryos, certain parts of which assumed a malignant growth. It has been suggested by various authors that such complex teratomata which are found in so preponderating a number in the sex glands may owe their origin

to a parthenogenetic development of ova. There was, however, some difficulty which prevented the general adoption of this view. There was not known any case in which the egg began to develop spontaneously within the ovary, particularly in mammals. The large majority of pathologists inclined therefore rather toward the adoption of the Bonnet-Marchand hypothesis that such teratomata are due to aberrant blastomeres.

Within recent years, however, we have succeeded in demonstrating that a parthenogenetic development of the egg in the mammalian ovary may actually occur. We have observed such a condition in a considerable number of cases in the guinea-pig. While parthenogenesis usually leads to the formation of embryonal placenta, thus explaining the occurrence of chorion epitheliomata in the sex glands, in two cases the production of typical embryonal tissue in the more restricted sense has been observed by us. There can therefore be no doubt that parthenogenetic development of the mammalian ovum within the ovary does actually take place and that it is a relatively not rare occurrence in certain species. This provides a basis of fact for the interpretation of embryonal tumors in the germ glands as being due to parthenogenetic development of ova within the follicles. There exists, however, a difference in different species in the readiness with which eggs mature in the ovary, such a maturation being apparently common in the guinea-pig and difficult in the rabbit. We may therefore expect that the frequency with which ovarian teratomata are found should vary in different species. In guinea-pigs we could show that such parthenogenetically developing ova do usually not change into teratomata such as they have been observed in man, but that they are invaded and gradually superseded by the host connective tissue before they have had a chance to develop into tumor-like masses.

It has now furthermore been established that an extensive migration of germ cells within the embryo takes place at an early stage of development. Thus it is conceivable that some of the embryomata which we find in places far removed from the ovary may be due to such a migration of germ cells which failed to reach their proper place.

There can, however, be little doubt that not only eggs but also parts of the embryo may, as a result of abnormal conditions, develop abnormally and give origin to teratomata and mixed tumors. It has usually been assumed that a detachment of embryonal cells from their normal environment is necessary for this purpose. Especially the recent investigations of Werber and Stockard have shown that even without such a separation, through toxic action (Werber) or a mere retardation in development (Stockard), embryonal parts whose development is usually coördinated may become independent of each other and may at relatively late stages of embryonic development give origin to twin

and monster formation. Thus we may assume that abnormal metabolic processes or other conditions which retard development at a certain place and at a critical period of development may cause embryonal malformations, teratomata or mixed tumors. But neither parthenogenetic development as such nor the formation of embryonal abnormalities through a slowing down of development can in themselves sufficiently explain the origin of cancer. Embryonal tissues which have been experimentally separated from their normal environment through transplantation behave in certain respects like normal embryonal tissues. They grow rapidly, differentiate and with progressive differentiation their development becomes slower; at last it ceases, and now the host tissue invades the transplant and a retrogression of the embryoma sets in. Askanazy, however, observed three cases in a series of approximately 150 experiments, in which the embryomata in the rat developed into cancers. These three cases were experiments in which the embryomata had persisted in the host for a much longer period than they usually do after transplantation. We may assume that in these cases abnormal stimuli had a chance to act on the embryonal tissues. Abnormalities in embryonal development or parthenogenesis as such are not sufficient to produce cancer; they merely prepare a favorable substratum on which additional stimuli may act. And it is the latter which call forth the development of cancer in these cases.

It is possible that in certain cases a changed environment as such may supply the stimulus which is needed in order to increase and prolong the proliferation and migratory energy of embryonal cells. In mammals, as we have seen, subcutaneous or intraperitoneal transplantation does not usually supply a sufficient stimulus for embryonal cells. If very early embryonal stages are transplanted they perish in the large majority of cases; but in one case we succeeded in the guinea-pig in producing thus the beginning of a peritoneal pregnancy.¹ Now, mammalian embryonic cells are adapted to growth within a living host organism. In animals in which the embryos develop normally outside the body, transplantation into an adult animal might perhaps supply a change in the environment large enough to produce profound stimulation of the cell activities. Experiments have, however, shown that in birds embryonic transplantations produce the same result as in mammals. Just as through transplantation in the rat and mouse, so through transplantation in birds embryomata are produced which have only a temporary existence. In amphibia, on the other hand, according to the recent experiments of Belogolowy,² injection of embryos in an early stage of development does not lead to the

¹ Loeb, Leo: Proc. Soc. Exper. Biol. and Med., 1914, No. 3, vol. xi; Biol. Bull., 1915, xxviii, 59.

² Belogolowy, G.: Archiv f. Entwicklungsmechanik, 1918, xliii. (It has been impossible for us to procure the original paper.)

development of typical embryos, but in certain cases to monstrosities. Various tissues proliferate irregularly and independently of each other. Plasmodia and irregular cells, not unlike sarcomatous cells, may penetrate into the host tissue and destroy the host organism as late as five or six months after transplantation. Here, apparently, certain similarities to cancerous growth are obtained. Whether a real cancer was produced, whether the growth energy continued undiminished without any farther differentiation, cannot be determined on the basis of the incomplete report of this work which is at our disposal. It is possible that in contact with the tissues of an adult organism cells which are in an early stage of embryonal development become transformed into plasmodia and syncytia and penetrate into the host, in a way similar to that we have described in the case of parthenogenetically developing eggs within the ovary. At that time we came to the conclusion that it is the contact with strange tissues which causes the transformation of embryonic cells into embryonal placenta.³ It is possible that under the influence of the stimulus of the strange environment a similar transformation takes place also in amphibian embryos and that the infiltrative growth continues and that thus a growth resembling in its effects a chorioepithelioma may be produced. At the same time the strangeness of the environment may, in so far as it does not lead to the destruction of the tissue, produce a desequilibrization, a severance of the mutual connections which exist between constituents of the embryo and which normally coordinate the development of parts to a whole, and thus duplication of certain parts of the embryo, similar to the result obtained in embryos through the action of certain poisons or through changes in temperature, may be brought about.

(e) *Age.* The relation between the age of the individuals and the frequency of cancer is not as simple as it is often assumed to be. Cancer may appear in young individuals. This is especially the case in those cancers which are due to transformation of embryonal into cancerous tissues. In some cases, however, the period of latency of these tumors may be considerable. The majority of those tumors which are due to stimulation of adult tissues appear in later life; this holds good in the case of human as well as of animal cancers. Thus we found in a statistical study of cancer in cattle, which we undertook twenty years ago, that the large majority of these cancers appeared in old cows. In mice also the incidence of mammary cancer increases, on the whole, with increasing age. This rule, however, does not preclude the fact that in man as well as in animals these same tumors may appear at a very early period of life. The number of mammary cancers which is found in young mice is indeed very considerable. The age at which the incidence

³ Loeb, Leo: Arch. f. Entwicklungsmechanik, 1911, xxxii, 662.

is greatest differs furthermore in the case of different strains of mice and this age character is just as much inheritable as the frequency of cancer in a particular strain. The age curve of frequency of cancer differs also in the case of different kinds of cancer. The age factor has therefore only a subsidiary significance in the etiology of cancer. The probability that long-continued stimulation leads to cancerous transformation must, of course, increase with increasing duration of life of the individual. Thus cancer must become more frequent with increasing age notwithstanding the better conditions for growth which young organisms and tissues offer. Cancer has this characteristic in common with many other diseases, where likewise the incidence increases with increasing age and the mortality as a whole shows a similar curve.

There is, however, still a problem concerning the age incidence of cancer which awaits solution. We have seen that it is accumulation of physical or chemical stimuli which causes cancer. These stimuli may originate in the outside world or in the inner environment of the cells within the individual. We have shown experimentally that in the case of these inner chemical stimuli (internal secretion) the quantity of the stimuli which is active in a given time may influence the cancer age. In part then we may refer the cancer age to the action of the environmental stimuli. It is, however, possible that in addition changes within the tissues which are characteristic of old age may tend to enhance the chances for cancerous transformation. It may be, as I pointed out on a previous occasion, that the changes characteristic of old age may place the cells into a new environment. Horst Oertel expresses the view that cells which are injured might be especially liable to undergo cancerous transformation, and Goodpasture has recently drawn attention to the frequency with which multiple tumors appear in dogs which have reached old age. At present we must regard it as problematical whether in addition to the cumulative action of external stimuli such internal factors play a part in the origin of tumors. If old age changes should bring about such an effect, an environmental change would in this case act as a growth stimulus. The environmental change which would produce such a transformation and lead to a proliferative reaction on the part of cells, may or may not have an injurious effect on the cells which it influences. If it should have such an injurious influence, it would be an adventitious, not an essential connection. Indeed, if these injurious by-products of the interference exceed a certain limit, the proliferative response of the tissues does not occur. Most of the tissues are constituted in such a way that within certain limits changes of environment of various kinds do not depress the cells but call forth a response which indicates increased activity.

(f) *Contact of normal tissues with cancerous tissue* may cause the transformation of the former into cancerous tissue. Thus may be

produced what we designated as "contact-combination tumors." Such a transformation of normal into cancerous cells in contact with cancerous tissue has been observed in the case of spontaneous tumors of man and animals as well as in the case of transplanted cancers. Primary carcinomatous tissue has called forth in many cases the transformation of connective tissue into sarcoma and in some cases the transformation of adjoining normal epithelium of a different kind into carcinoma; thus "combination tumors" originated. Ehrlich published such an observation more than twelve years ago. At the same time we observed sarcomatous transformation of stroma after transplantation of mammary carcinoma in waltzing mice as early as in the first generation of the transplanted tumors, and subsequently in another case we found a transformation of epidermis into squamous-cell carcinoma in contact with a mammary carcinoma. Some authors believed that the tissue which had been interpreted as sarcoma, was only a pseudo-sarcoma, and consisted in reality of spindle-shaped epithelial cells. However, there cannot be any doubt that in such cases we have actually to deal with a proliferation of true fibroblasts, and in accordance with this interpretation is the recent observation of Woglom, who found the formation of cartilage in such a contact-combination tumor.

We have certain analogies for such contact action in the case of embryonal and also of adult tissues. Thus substances given off by the optic disk may call forth proliferation of the epidermis with which it is in contact, the proliferating cells giving origin to the lens. In the mammary gland the condition of the stroma depends upon the state of activity of the gland tissue. Activity of the gland tissue produces a stroma rich in fibroblasts and a resting gland induces a fibrous transformation of the stroma. Around gland ducts which are metabolically relatively inactive, the stroma is usually fibrous. It is therefore probable that the cancerous transformation of normal tissue in contact with cancer is another instance of the stimulating effect which one tissue may have upon another normally. The difference in the normal and pathological cases is mainly a quantitative one.

(g) *The Possible Significance of Microorganisms in the Etiology of Cancer.* When microorganisms were discovered as the cause of infectious diseases, some of which were associated with a noticeable tissue proliferation and with the formation of secondary foci, comparable to metastases, and when it was shown that certain microorganisms can call forth even proliferation of epithelial structures, the conclusion was drawn that cancerous growth may likewise be due to microorganisms. This conclusion seemed to be confirmed by the presence within the tumors of structures which resembled various unicellular microorganisms. Another fact which seemed to

point in the same direction was the so-called endemic occurrence of cancer in certain animals. It was referred to eage infection.

At present neither of these arguments is accepted, at least so far as the large majority of pathologists is concerned. No unicellular microorganisms have been found in cancer; no agent can be separated from cells in mammalian tumors. The structures taken to be parasites were shown to be due to cell degenerations and phagocytoses. The endemic occurrence of cancer is due to two factors: (1) to the hereditary transmission of cancer in certain strains of animals, and (2) to the introduction of metazoic parasites which infect a certain class of animals at a particular place and act as a temporary stimulus of the tissues, and which later disappear after the tissues have been converted into cancer. This applies, for instance, to the cancer in rats observed by Fibiger.

The arguments which speak against the significance of microorganisms in the etiology of the large majority of mammalian tumors seem to be convincing. Observation shows that human cancer is in many cases due to the long-continued action of growth stimuli on cells. Occasionally a growth stimulus may call forth the sudden appearance of cancer. Experimentally cancer has been produced through the action, physical or chemical, of growth stimuli and has been prevented through the withdrawal of chemical growth stimuli (mammary cancer of mice). It has been shown that no immunity can be produced against auto-cancers (spontaneous cancers) but only against homoiocancers (transplanted cancers). Immunity against homoiocancers can be produced through normal tissues of the same species. These facts prove that we have in these cases to deal not with an immunity against an extraneous organism but against tissues growing abnormally.

Through the action especially of chemical growth stimuli normal tissues can be transformed into cancerous tissues without the intervention of ulceration. Injection of any known microorganism does not produce cancer. It is therefore extremely improbable that the cancers which originate after long-continued stimulation of normal tissues should be due to the accidental invasion of the tissues by a class of microorganisms which have not been observed at places where they would have to enter the tissues, and which would have to be ubiquitous, in view of the great number of animals which can be made to be cancerous. We would, moreover, have to assume that specific microorganisms exist in the case of different varieties of tumor in view of the fact that cancer has to some extent a specific character. Such microorganisms should, moreover, be able to gain access to the embryonal tissues which form in a certain number of cases the matrix of the tumors. All these considerations make it very improbable that in addition to the causes of cancer enumerated above there are other factors, which while leading a hidden existence would be the really important ones, in contra-

distinction to the aforementioned causes which would only serve as an opportunity for the microorganism to enter the host tissues.

Yet it is conceivable that the same kind of cancerous growth which is produced through a change in the chemism of the cell as the result of the long-continued effect of growth stimuli, might also be called forth through the action of an extraneous stimulus constantly associated with the cells; such a stimulus might be furnished by a substance given off by a microorganism. There are certain sarcomata of fowl in which Peyton Rous discovered an agent separable from the tumor cells through filtration and other means which had failed in the case of mammalian cancers. Injection of these agents into other fowl causes the development of tumors identical with the original ones. These tumors are metastasizing and transplantable. After transplantation of tumor tissue transplanted cells remain alive and give origin to the new growth. An immunity against these tumors can be produced, but it is an immunity against the agent and not against the tumor cells, in contradistinction to the immunity obtained in the large majority of other and particularly of the typical mammalian tumors, where we have to deal with an immunity against tumor cells. Certain sarcomatous tumors found in hares and perhaps a certain sarcoma found in dogs resemble in certain respects the chicken sarcoma, and although a direct separation of tumor agent and tumor cells has not been accomplished in the latter cases, the etiology may be similar.

In the case of the fowl tumor the agent seems to be specifically adapted to the organism of fowl or of birds in general. In this sense we are inclined to interpret the fact found by Rous that only in certain birds and not in rabbits is it possible to produce an immunity against the agent of the chicken sarcoma. It is not improbable that in the case of these sarcomata we have indeed to deal with proliferative processes called forth by microorganisms accompanying the cells and specifically adapted to the latter, although the possibility cannot yet be quite excluded that the agent may be a substance produced by and separable from the proliferating cells.

In plants Erwin Smith has discovered a bacterium which causes a gall to assume invasive properties. This bacterium acts through the production of an apparently simple substance which induces the proliferation of the plant cells.

It is therefore possible that while in the majority of cancers often repeated stimulation of tissues leads to a long continued or even perpetual increase in the intensity of those metabolic processes which cause cell proliferation and cell movements, in certain sarcomata the same effect is produced through a constantly acting extraneous chemical growth stimulus, supplied by microorganisms and not as in the case of the majority of cancers through the own metabolism of the cancer cells.

Some General Considerations. We have seen that all the factors which in various ways either by chemical or physical means increase the proliferative energy of cells may act as causes of cancer; these conditions are not different from those growth stimuli which lead to regenerative and what might be called correlative growth in normal tissues; added to these factors are in certain cases factors residing within the cells, which make these cells more responsive to outer growth stimuli, thus providing a sensitization which in other cases is furnished by sensitizing substances carried to the cells from other organs. We concluded that in order to lead to the formation of cancer in many cases several of such factors must coöperate. Some of these factors are hereditarily transmitted in a certain graded quantity from generation to generation, while the other factors are variable and extraneous. All these factors have one characteristic in common: They all increase the growth energy of normal tissues either directly, or indirectly, the latter by sensitizing the tissues to the action of growth stimuli.

We have previously shown experimentally that a combination of such diverse growth stimuli can under certain conditions accomplish results which are very much greater than the ones produced by either of these factors alone. In the case of the maternal placenta two factors coöperate. In the first place a substance is given off by the corpus luteum. It calls forth only a very slight proliferation of the uterine mucosa, but it sensitizes the latter in such a way that the subsequent application of an external stimulus (a foreign body, ovum), which in itself would likewise call forth only a very slight reaction, leads to the production of tumor-like masses, placenta and placentomata (deciduomata). In a similar way heredity might in some cases act by supplying sensitizing substances which make cells receptive to the effect of outer growth stimuli. Thus in xeroderma pigmentosum we find an abnormal sensitiveness of the skin to the action of outer stimuli, probably light, which causes a sequence of changes leading ultimately to the production of cancer and not unlike those observed in experimental cancer in animals.

There is some reason to assume that a reciprocal relation exists between those factors which may be classed as hereditary and those which are extraneous growth stimuli. It may perhaps be expressed through the formula $H + S = C$, where H represents hereditary factors and S external growth stimuli. The greater the quantity of one kind the less is needed of the other kind in order to produce cancer. Thus it seems that roentgen rays can ultimately produce cancer in all persons whether or not they are hereditarily predisposed to cancer, provided the roentgen rays have a chance to act over a sufficiently long period of time. Of course as far as the quantitative aspect expressed in the equation is concerned we have at present to deal merely with a hypothesis. We found that given a certain hereditary predisposition a quantitative relation seems to

exist between the amount of internal secretion given off and the frequency of cancer which resulted. In this case a quantitative relationship is not merely assumed, but has been definitely proved.

We conclude that various growth stimuli including those of a regenerative character may gradually bring about a change in the cell equilibrium. The normal cell equilibrium which is characterized by a definite proliferating energy may pass through several transitional stages into an equilibrium of greater proliferative and kinetic energy. This is not only a change in intensity but also in duration. In the last stage the change has apparently become permanent.

In the normal organism we find a complex interaction of various tissues. They exert upon each other under certain conditions a restraining and under other conditions a stimulating effect.

Alteration of these relationships and introduction of an abnormal environment leads usually to only temporary changes in the cell equilibrium, to growth processes of a regenerative or correlative character; this applies to changes affecting embryonal as well as adult tissues. But through frequent repetition of these changes which act as stimuli the cell equilibrium may be changed in such a manner that the alteration continues over a long period of time or has become permanent. In different cases the quantity of stimulation which is needed for this effect to take place varies. We may call such a change in cell equilibrium, inasmuch as it is transmitted to successive cell generations and may appear as a well-defined transformation in the character of the cell, a mutation, but it would be a mutation of somatic cells. This somatic mutation is, however, in part at least, dependent upon conditions transmitted through the germ cells.

The basis of this transformation in cell equilibrium may be conceived as a change in cell metabolism, during which substances are produced which maintain the alteration in cell metabolism on which the acceleration in growth and the increase in motility depends. It is conceivable that in certain cases a similar constant alteration is produced through a stimulus reaching the cell from an extraneous source; a microorganism might perhaps be able to supply such a stimulus.

The various kinds of transitory increase in growth and kinetic energy as exemplified in regenerative, embryonal, correlative growth and in the combination of correlative and regenerative growth (the development of deciduomata) are probably the expression of a kind of metabolic cell change similar to the one observed in cancer. And tissues in which correlative or regenerative growth processes occur are therefore liable to become cancerous, while those which are not accessible to the former are not likely to undergo the cancerous transformation. There are, however, differences in intensity and also differences of a secondary character between the kinds of normal increase in growth energy and between

cancerous growth. In the latter, as the result of the abnormal conditions in the cells which are reached by the stimuli, structural abnormalities are produced.

We have attempted to correlate the most important facts which have a bearing on the etiology of cancer. We see that while of a composite character the various factors, as far as they are known to us, have one characteristic in common: they tend to increase the proliferative energy and motility of cells which are not yet cancerous. The picture thus presented is more complex than the one which we meet in the "theories of cancer" to which so much attention has been given in the literature. In the case of a "theory of cancer" usually one or the other of the factors underlying cancer has been considered with the exclusion of all the factors. Deductions based on the histological characteristics which were usually not accessible to experimental analysis formed often the basis of such theories. Thus a simplification was attained which was more apparent than real.

Equally prominent in the literature has been the discussion whether or not a certain new formation is to be classed as a cancer. The answer given usually depended on the "theory of cancer" to which the author subscribed. A definition of a condition cannot be more definite than our knowledge of this condition; otherwise the definition produces an artificial restriction to the search for new relations. A definition is therefore perhaps of less importance than is often attached to it. It is essentially a summary of our knowledge of a phenomenon. Cancer is abnormality of growth. Primarily it is a disturbance in the equilibrium of the individual, not through toxins but through an increased proliferative activity of the cells which is usually associated with an increased motility. This increase is long continued and often permanent. It is in all probability in the large majority of cases due to changes in cell metabolism, which are of such a character that they propagate themselves. In some cases the same effect may perhaps be produced through extraneous causes, such as microorganisms.

THE TREATMENT OF THYROID AND OTHER ENDOCRIN DISTURBANCES AS VIEWED BY THE INTERNIST.¹

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Mrs. G. C., a farmer's wife, aged fifty-nine years, was brought to the hospital by her family physician. She complained of a throb-

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, December 15, 1919.

bing, beating sensation in the abdomen and also of general weakness. These symptoms came on gradually in the past six months. They had their inception apparently from a nervous shock. The patient's only son had died rather suddenly following an operation for a ruptured appendix and a few days later her only grandchild died of influenza. On further inquiry it was found that nine years previously, while the patient was passing through the menopause, her only daughter died very suddenly, and that following this death she had what was then called a "nervous breakdown," a condition thought to be similar to her present attack.

The patient was found to be 37 pounds below her usual weight. The skin was moist. The pulse-rate was 132 and easily accelerated; the heart action was violent. There was tremor of the tongue and hands. The hair was brittle and the eyes prominent. A slight bogginess of the isthmus of the thyroid could be felt. Practically every symptom of hyperthyroidism was present.

This is a familiar picture which resulted from the tragic episodes which came to the household over which the patient presided. In a rather intensive study of the case, definite evidence of an unbalanced endocrin system in which the thyroid gland was the chief factor was found. In addition to the very evident symptoms the examination brought out the fact that carbohydrate metabolism was disturbed. A subcutaneous injection of $\frac{1}{2}$ c.c. of 1 to 1000 adrenalin solution ("Goetsch test") produced a glycosuria, though it aggravated the thyroid symptoms only slightly. A carbohydrate tolerance test also brought sugar to the urine, even though there was no previous hyperglycemia demonstrable. While the patient was resting in her changed surroundings the thyroid lost its boggy feel, body weight was increased and the most prominent symptoms, especially the tachycardia and anxiety, disappeared.

This patient, aside from illustrating a large and increasing group of cases, also demonstrates how profound and disabling such symptoms may be without there being present very definite physical signs suggestive of definite pathology; and it also brings out the question whether there might not be an early stage in the course of the disturbances of the endocrin system, where a comprehension of what is taking place, or is about to take place, may lead to earlier recognition and consequently more satisfactory treatment. It is for the purpose of presenting this idea that the present consideration from the viewpoint of the internist is attempted.

It is, of course, axiomatic that if a disease is to be recognized and dealt with at its earliest inception there must exist a thorough knowledge of the etiology as well as of the pathology and of the clinical manifestations. Unfortunately of diseases and disturbances of the endocrin system we know comparatively little, practically nothing definite, of the etiology, and we have only confused ideas of the associated pathological processes. Compared with our present-

day knowledge of such a well-known disease as typhoid fever we know very little about the diseases of the glands of internal secretion, and are therefore at a great disadvantage and no doubt show a great confusion of opinions. There is not yet that coördination in effort and ideas of the laboratory workers, of the clinician and of the surgeons, all of whom are intensely interested in the problems which the subject presents. In the last decade or so much information has accumulated: (1) Because of the fact that endocrin disturbances are more generally recognized by the clinician; (2) their relation to disease in general and to definite pathology is being established, and theorizing has been displaced by more earnest laboratory investigation. The recent great war with all its strain and anxiety, resulting in so-called shell-shock, effort syndrome, neurocirculatory asthenia, all of which may be manifestations of endocrin disturbance, has made the problem really acute, and it is well to pause at this time for a moment to review the present status and to consider the foundations for our faith in the procedures we are advocating when we speak of the treatment for a certain symptom-complex referred to the endocrin system. In this consideration the diseases and disturbances of the thyroid gland are of particular importance.

In such a review we must acknowledge our debt to the laboratory worker and his discoveries. It will be interesting, and probably helpful, to refer briefly to some of their epoch-making revelations, because from them will be seen at once the relation which the several glands of the endocrin system bear to each other, and it will also show where the clinician receives his greatest help and in what direction his efforts will likely prove most fruitful. Only brief reference can be made to early laboratory results which have more recently shown the coördination of the endocrin system and how delicately this system is balanced.

THE SUPRARENALS AND THEIR SPECIFIC SECRETION. It was in 1841 that Magenda told his students that he had nothing to say about the suprarenal bodies, because the capsule is no longer considered as a secreting body. Just fourteen years later (1855) Thomas Addison described the disease which bears his name, and this marked the beginning of clinical work in relation to the suprarenal glands. In 1902 J. Takamine published the work of Aldrich and himself,² giving a description of a crystalline compound and its clinical formula, which they isolated from the suprarenal gland. Later, Stolz, followed immediately by Abel, produced this crystalline form—adrenalin—synthetically. This substance figures largely in developing our knowledge of the interrelation of the ductless glands. With it we can produce most profound circulatory disturbances: can, under certain conditions, activate the thyroid gland and can

² Jour. Am. Med. Assn., January 18, 1902, p. 153.

unbalance carbohydrate metabolism. It has become a definite therapeutic agent and, administered under certain conditions, also gives diagnostic information.

THE THYMUS GLAND AND ITS RELATION TO THYROID DISTURBANCE. In his Harvey lecture in March, 1914, Halstead called attention to the belief that the thymus gland plays an important part in Graves's disease. He said: "It has been estimated, as a result of non-operative clinical examination, that in about 40 per cent. of all cases of exophthalmic goiter the thymus is present." He refers to 500 patients with Graves's disease operated with approximate cures in 60 per cent. The exophthalmos and the typical blood picture seemed the most difficult conditions to overcome, even when the major symptoms had largely subsided, but both conditions yielded when the thymus was considered properly. Halstead then refers to the relation of the thymus to the thyroid as noticed by other observers, and says, from the facts gleaned at the autopsy table, from experiments on animals and above all from the results following primary thymectomies, we have convincing evidence that the thymus gland may play an important part in Graves's disease. Two months later he referred to the treatment of the thymus gland with roentgen rays in certain selected cases of Graves's disease and reported his experience in a subsequent paper. While the coördination of the thymus and the thyroid glands, which Halstead suggested, has not proved so generally convincing as it promised, his work led to the demonstration of the effect of the roentgen rays in thyroid disease, whether through the thymus or direct on the thyroid.

An interesting case which occurred in my experience, apparently bearing upon the relation of the thymus to the thyroid, is as follows: A man whom I had known for a number of years consulted me about five years ago on account of a tickling in his throat. A physical examination showed nothing, but rather definitely prominent eyes. An examination by a nose and throat specialist was negative. The hacking cough continued, however, and was finally so severe that the patient could not lie down without bringing on a violent paroxysm of coughing. He was unable to sleep in a prone position. About this time he had a severe attack of acute tonsillitis, which was followed by tachycardia, which could not be explained except as probably due to the preceding acute infection. Graves's disease was considered, as many symptoms were suggestive. The thyroid, however, was not enlarged. A roentgen-ray examination of the chest, especially of the mediastinum, showed an enormous enlargement of the thymus gland. It is possible that this was present in a lesser degree from the first and accounted for the hacking cough. It was suggested that the acute infection led to a rapid enlargement of the thymus and that the symptoms of Graves's disease, which we then recognized clearly, were due to the effect of the thymus upon

the thyroid. The symptoms, including the tickling cough, were relieved entirely by treating the thymus with roentgen-ray applications. The patient has been well now for nearly three years. A roentgen-ray examination of the mediastinum following the treatment showed a great reduction in the thymus gland. The excellent result in this case is another reason for reporting it. It is possible that the roentgen-ray applications to the thymus had a direct action upon the thyroid as well, and that the change in size of the thymus was simply coincident. I am all the more willing to consider the case in this way since reading the recent article by Drs. Edward Park and Roy D. McClure³ in which they conclude, from an extensive review of the literature and after painstaking animal experimentation, that destruction of the thymus function fails to show an effect on the thyroid gland. While the thymus may not bear the relation to the thyroid which Halstead suggested, after all his work called attention to the effect of the roentgen rays upon the thyroid secretion, and added greatly to the therapeutics of thyroid disease.

THE PITUITARY BODY AND ITS SECRETION. The work of Marie, of Schafer and later of Howel called attention to the hypophysis cerebri, in the chain of the glands of internal secretion, as a "vitally important organ." It was not, however, until the masterly work of Cushing⁴ appeared that it was at all appreciated what pathology may occur in the pituitary gland, and what clinical and what physiological disturbances may follow. There resulted from the studies of this gland, as from that of the suprarenal, another addition to our therapeutic armamentarium. The effect of pituitrin upon the gravid uterus and upon the relaxed unstriated muscles in general is well known. More recently the effect of pituitrin on urinary secretion has been brought to our attention. A striking demonstration of the effect of pituitrin on diabetes insipidus is presented in the following case: A sixteen-year-old girl consulted me on account of sleeplessness and of being occasionally mentally confused. In the course of the history it was found that the patient had a polyuria, passing as much as 5 liters of urine in twenty-four hours. She also had polydipsia. This was largely responsible for the sleeplessness. After careful investigation a diagnosis of diabetes insipidus was made. Pituitrin was given daily and in forty-eight hours the urinary output was reduced to 1½ liters. The intense thirst disappeared and sleep was natural. The symptoms were later controlled by smaller doses given less frequently. The limitations of this treatment are, of course, generally recognized, and yet it is a good example of the profound specific effect of a substance elaborated in the hypophysis cerebri. In an article in the *Quarterly Journal of Medicine* (April, 1919), Kenneway and Mottram, of the Middlesex

³ The Results of Thymus Extirpation, *Am. Jour. Dis. Children*, November, 1919.

⁴ Bull. Johns Hopkins Hosp., May, 1910.

Hospital, London, recorded the antidiuretic effect of pituitrin subcutaneously injected in normal individuals as well as in those having diabetes insipidus. It would seem, however, that this observation will need further investigation.

THE PANCREAS AND ITS INTERNAL SECRETION. The role of the islands of Langerhans in relation to carbohydrate metabolism, and especially the histological changes which take place in diabetes mellitus, was first definitely brought to our attention by Opie in 1900.⁵ Since that time the work upon the pancreas has been prodigious and has resulted in a more rational view of the relation of diabetes mellitus to the pancreas. McCallum⁶ called attention to the actual hypertrophy of the isles in severe cases of diabetes mellitus. And later Allen⁷ demonstrated definitely the relation between the disease of the pancreas, especially of the isles of Langerhans, and diabetes mellitus, and suggested a rational treatment, which Joslin, from a clinical standpoint, subsequently made practical. Allen and Joslin's work is intensely practical and is of real value to the clinician. The emphasis which Allen has put upon early recognition of physiological disturbance of the isles of Langerhans and prompt definite interference is applicable not only in diseases of other organs of the endocrin system, but may be of value in those diseases in general whose early symptoms might be easily overlooked.

It would be interesting to speak of the ovaries and their specific secretion, of the parathyroids and of other glands of the endocrin system, but I shall now direct my remarks more specifically to that laboratory work which has led the internist to more rational procedures in diseases and disturbances of the thyroid gland. The first description of thyroid disturbance by Graves, in 1835, is, of course, a matter of history, and the laboratory work which led to the extraction of a substance from sheep's thyroid, which when given in sufficient dose reproduced the symptoms of Graves's disease. The important place which thyroid extract took as a therapeutic measure is well known to all. Very little of value has been added to the definite clinical description which characterizes Graves's first paper. I shall refer only to the recent laboratory investigations and their bearing upon our present concept of thyroid disturbances, especially in so far as early diagnosis and the treatment therefor is concerned.

THE DISTURBANCE OF BASAL METABOLISM IN HYPERTHYROIDISM. We are indebted to Du Bois⁸ for first successfully calling attention to the striking change which takes place in metabolism in the thyroid case. In his paper Du Bois says that in a study of the basal metab-

⁵ Jour. Exper. Med., 1901.

⁶ AM. JOUR. MED. SC., 1917, cxxxiii, 432.

⁷ Glycosuria and Diabetes, Harvard University Press, 1913.

⁸ Arch. Int. Med., 1916, xvii, 915.

olism in hyperthyroidism it becomes apparent there is an increase in metabolism in proportion to the severity of the disease. Very severe cases show a metabolism 75 per cent. or more above the average, severe cases 50 per cent. or more, moderately severe and mild cases show an increase of less than 50 per cent., while a few mild and several atypical cases, or cases in which operation has been performed, are within normal limits. The degree of tachycardia, goitre, exophthalmos and mental irritability are roughly proportional to the increased heat production. At least a part of the tachycardia is due to the increased metabolism, and perhaps it might be possible to reproduce the extreme tachycardia, the cardiac enlargement, emaciation and mental irritability if we are able to stimulate the metabolism of normal men for twenty hours a day over a period of months or of years.

These observations of Du Bois and his conclusions have become so generally recognized that it is now necessary to make metabolism observations before a diagnosis of hyperthyroidism is accepted, or at least before a reliable and safe prognosis can be made. It would be interesting to note, by a series of investigations, whether the basal metabolism is changed in any way in those early cases in which the subcutaneous injection of adrenalin seems to develop a so-called potential hyperthyroidism. Studies in metabolism are now being made in the cases of so-called effort syndrome which may result in differentiating these cases definitely from hyperthyroid cases or which may show that they manifest early symptoms of the exophthalmic goitre syndrome. I am of the opinion that the latter may be found the true interpretation, though I believe this is contrary to the opinions of those who have had large opportunity for observation in the neuropsychiatric division of the army.

Barring the slight temporary boggyiness of the thyroid, the case to which we referred at the beginning of this paper, came very near corresponding to the neurocirculatory-asthenia syndrome instead of to that of hyperthyroidism. It will require more definite laboratory and clinical work before this point of differentiation can be clarified.

THE INNERVATION OF THE THYROID GLAND. This was presented in an article by Cannon,⁹ entitled "Conditions Affecting the Secretions of the Thyroid Gland," in which he concluded, after describing his methods of observation, that "The nerves distributed to the thyroid cells belong to the sympathetic and not to the vagal supply and that their effects are not indirect through alterations of blood flow: indeed, that they are true secretory nerves. The thyroid gland is subject to that division of the nervous system which is brought into action in emotional excitement and which causes adrenal secretion. It is probable, therefore, that the thyroid, like the adrenal,

⁹ Boston Med. and Surg. Jour., 1916 clv, 562.

has, normally, functions which are performed in times of critical emergency. It may be that such an emergency function is an exaggerated form of the routine activity of the gland." Cannon's work has been severely criticized, but it has stimulated research on the innervation of the thyroid and will no doubt result in bringing out the real facts, which is, of course, the object of all scientific investigation. The latest word on this subject is probably that of C. A. Mills,¹⁰ in which he affirms the lack of secretive function of the sympathetic fibers of the thyroid gland.

THE ISOLATION IN CRYSTALLINE FORM OF AN IODIN COMPOUND FROM THE THYROID GLAND. In an article by Dr. E. C. Kendell, of the Mayo Clinic,¹¹ he announces the discovery and separation among other substances, of a purely crystalline compound containing 60 per cent. iodine. It appears to be an iodo-di-hydroxy-indol. Administration of this substance in a human being produces a rapid increase in pulse-rate, gain in vigor and increase in metabolism and nervous irritability. Given in excess, toxic symptoms are produced. The amount of iodine compound required to produce toxic effect is exceedingly small. He believes it plays an important role in the production of the symptoms of exophthalmic goitre. Kendell says, further, that in exophthalmic goitre two abnormal conditions exist: (a) The secretory capacity of the gland is greatly increased, and (b) the reservoir capacity of the gland is greatly decreased.

The use of iodine in goitre is a procedure to which our attention was called many years ago. The results of Kendell's work impress one very much with Marine and Kimball's observations, as reported in the *Archives of Internal Medicine*, July, 1918, "The Prevention of Simple Goitre in Man." They had the opportunity of observing 1080 girls in the Akron public schools, with reference to the effect of administering iodine. They concluded (1) that simple goitres may be prevented by the administration of small amounts of iodine; (2) simple goitres disappear or are markedly decreased by the use of a small amount of iodine given internally; (3) there is no danger of producing toxic conditions, such as Basedow's disease; (4) simple goitre is probably the easiest of all known diseases to prevent.

A TEST FOR DETERMINING "POTENTIAL HYPERTHYROIDISM." Dr. Emil Goetsch has suggested a unique procedure for determining the potential possibilities of the thyroid in the particular individual. The principle and procedure of this test are no doubt familiar to all. One-half cubic centimeter of 1 to 1000 solution adrenalin is injected subcutaneously and subsequent observations are made upon pulse-rate, blood-pressure, urinary secretion, blood sugar and objective and subjective symptoms. It has served a great purpose in our clinic, not only from a diagnostic and prognostic standpoint con-

¹⁰ *Am. Jour. Physiol.*, October, 1919.

¹¹ The Isolation in Crystalline Form of the Compound Containing Iodine Which Occurs in the Thyroid, *Jour. Am. Med. Assn.*, 1915, lxiv, 2042.

cerning thyroid conditions, but it has increased our interest in endocrin disturbances in general.

By way of improvement in technic we would suggest that the administration of the adrenalin be preceded by a preliminary course of hypodermics of sterile water. It gives the patient time to be accustomed to the hospital, to hypodermic medication and to the routine of close observation. We find the results much more reliable when this precaution is taken. The effect of adrenalin administered in this way and for this purpose, we feel, is subject to a number of interpretations. At present we believe we can recognize two or three rather distinct groups of cases as the result of the activating injection. One is a group in which the circulatory symptoms—tachycardia, palpitation and precordial distress—predominate; another in which the nervous symptoms, such as substernal distress, *i. e.*, globus, "internal tremor," trembling of the hands, restlessness and agitation are present, with scarcely any acceleration of the pulse-rate. And a third group, in which only disturbance of the carbohydrate metabolism occurs, as evidenced by hyperglycemia and mild glycosuria as the leading factors. In the case of the first patient whose history I presented the Goetsch test was negative in so far as an increase of the circulatory and nervous disturbances was concerned, but sugar was found in the urine, and a sugar tolerance test also produced a glycosuria and a hyperglycemia. When the patient was not under the effect of adrenalin there was no hyperglycemia.

We are of the opinion that many points will have to be cleared up before the full significance of the Goetsch test will be known. May it not be possible that with the Goetsch test we might find there is a stage in the course of the hyperthyroid condition, even preceding that of appreciably increased metabolism, in which the Goetsch test might be positive, and thus warn us of what is about to take place?

Enough has been said to justify the claim that we are in possession at present of data from the laboratory which has greatly stimulated our interest and increased our ability to recognize and diagnose early endocrin disturbances. It must be concluded that the internist who is in possession of the data to which meager reference has already been made should now be in a position to recognize the first alteration of function which points to disturbance or disease of the endocrin system, and should forestall by prophylactic measures the impending disaster. In the case of the thyroid, for example, where there is evident hypertrophy, one's attention should, of course, be called at once to the possibility of early symptoms of Graves's disease; but when there is no apparent hypertrophy the slightest symptom should receive careful consideration.

It is not the purpose of this paper to go into the details of the symptomatology, such as the definite loss of weight in spite of

unimpaired appetite, the increased amount of energy discharged, the physical and mental restlessness, the tremor, the loss of vascular tone, the acceleration of the pulse-rate and the so-called internal tremor to which the thyroid patient so frequently refers. It is intended rather to call attention to very early functional changes which may be recognized by certain tests, showing an unbalanced endocrin system. If these changes are taken at their face value and early treatment instituted the results in many cases would no doubt be different. Medical treatment would be more effective and the surgeon and roentgenologist would not need to be called so frequently as they are at present. This I believe to be especially true in so far as the thyroid gland is concerned.

In a paper by Dr. John H. Musser, read in Chicago in 1911, on Problems in the Treatment of Exophthalmic Goitre,¹² he says in his conclusions: "Finally, my conviction is that the surgeon does too much and the internist too little in the treatment of goitre." This was probably the last paper Dr. Musser read. With our present knowledge we would no doubt say, in addition to what Dr. Musser has said, that the internist besides doing "too little" does it too late. Nothing will clear up the goitre problem more satisfactorily and promise better therapeutic results than prompt recognition and establishment of early, definite and earnest treatment. Under such conditions a large proportion of cases will no doubt get well with so-called medical treatment. The fact, of course, must never be lost sight of that any pathology of the thyroid gland should receive the same consideration that similar pathology does in other parts of the body, with this difference, however: The far-reaching effect of suddenly disturbing thyroid secretion must always be kept in mind. If a cyst is present, or an adenoma, or a malignant neoplasm, it should be considered along the well-established lines which such pathology receives when it occurs in other parts of the body. And on account of our lack of knowledge of the etiology of exophthalmic goitre there must be no varying from the general principles which obtain in the treatment of any disease. Particularly is this true of the chronic infections due to local foci and of the acute general infections. We could all no doubt cite instances of the apparently very close relation of thyroid disturbances to diseased tonsils, infected sinuses or abscessed teeth. Unquestionably these conditions should all be taken care of on the basis of their own pathology, whether there is thyroid disturbance or not. This means, therefore, that surgery has a large field in diseases of the endocrin system, and especially in diseases of the thyroid.

In speaking of medical treatment, on account of the peculiar individual phases which each case may represent, it is best only to mention the principles upon which it is based. It is based upon the

¹² AM. JOUR. MED. SC., cxliii, 810.

principles established by those investigators to whom reference has been made. The disturbance of function of that nervous mechanism which Cannon, Mills and others have described must be controlled. This means rest in varying degrees. It may mean, also, very active medication, such as nerve sedatives—the bromides for example. The loss in weight which Du Bois has explained must be overcome. This means abundance of food—indeed, forced feeding. The disturbance of a certain secretion to which Marine and Kimball have called attention must be balanced by careful medication. This means measures to forestall or to correct a changed secretion. No one up to this day has better outlined a course of treatment, especially in so far as rest and forced feeding is concerned, than has Dr. S. Weir Mitchell in his plan of the rest treatment. The possibilities of restoring nerve function, mental balance and loss of weight by the proper application of the principles laid down by Mitchell is recognized by all. One need only read Mitchell's little book entitled *Fat and Blood* to get a definite outline and all the details of the rest treatment. It is especially applicable in the incipient and early cases of thyroid disturbance. The rest and feeding must be prolonged until the results are obtained and securely held.

The late Dr. Janeway, in discussing a collection of papers referring to thyroid conditions and the various treatments therefor, said: "I have seen that symptoms when recognized early permit of successful medical treatment in spite of the fact that for the patients studied nowadays in hospitals surgery is usually necessary. One of the reasons for difference of opinion between surgical and medical men is that we tend more and more to treat our patients in the hospital (where they arrive late). In private patients who will early cooperate, however, the medical man may accomplish cures which are permanent. Such patients must be carefully selected and more carefully managed."¹³

This brings us to the crux of the goitre question in so far as the treatment of all cases in whatever stage is concerned. It is the proper selection of cases, or rather the proper selection of the treatment, for the particular individual patient. Unfortunately, patients do not usually consult a physician in the early stage to which attention has been called. Prophylactic treatment is not always applicable. Yet patients must be cared for at whatever stage they present themselves. Early in my medical practice I determined upon a classification of goitre patients which has been very helpful to me, and which up to the present I have not seen fit to abandon. It furnishes a rather satisfactory working basis for the determination of the proper treatment in the individual patient. It does not preclude any classification, thus far suggested, of diseases of the thyroid gland based upon demonstrable and well-recognized pathology.

¹³ Janeway, T. C.: Boston Med. and Surg. Jour., 1916, clxxv, 685.

Patients having disease or disturbance of the thyroid gland are divided into four groups:

Group 1. Those patients having hyper- or hypothyroidism without any apparent pathological change in the gland. No change in the size or shape of the thyroid is demonstrable physically. These may be early cases in which later pathology will become manifest, or they may be well-advanced cases with no pathology of the glands. If one is keen in recognizing the early symptoms of thyroid disturbance this class may be large. The symptom-complex, however, is often remarkably definite if one will go after it. At other times a study of the basal metabolism and possibly the application of the before-mentioned Goetsch test may be necessary to confirm the suspicion. The treatment in these cases is definitely medical. I do not know of any attempts of treatment by roentgen ray in these cases, unless it be in those cases in which the thymus gland is enlarged. Surgery is not necessary.

Group 2. Those patients having an enlargement of the thyroid but in which from the age of the patient and the absence of certain symptoms the diagnosis of adolescent goitre may be made. It occurs in young girls about the time of the establishment of the menstrual period. It may also occur in boys at the age of puberty. The enlargement is usually temporary. There are, of course, notable exceptions. If any definite treatment is necessary it is medical. Usually time and careful prophylactic measures may prevent the hyperthyroid syndrome. The iodides in small doses or small doses of thyroid extract may be advisable. One of my cases was a notable exception: A young girl was brought to me at the age of twelve with a slightly enlarged thyroid. It had been noticed for about four years, or since she was eight years old. Advice had already been given that it was an adolescent goitre and would likely disappear in due time. There was no reason at that time for advising anything to the contrary, as there were no symptoms. The tonsils were diseased and removed without any untoward symptoms. Definite prophylactic treatment was instituted. When the periods came on at the age of fourteen there was no change in the size of the gland, but at the end of two years it was larger. No symptoms of hyperthyroidism were noticed, but the patient wished a lobectomy for cosmetic purposes if for nothing else. A partial lobectomy was done under local anesthesia. The right lobe and the isthmus were removed. It proved to be a parenchymatous hyperplasia. Within a year of the operation the remaining lobe enlarged rapidly and symptoms of hyperthyroidism were noted. A second operation was considered, but finally it was decided to apply roentgen rays. After eighteen applications by Dr. Russell H. Boggs the swelling had about disappeared. This was three years ago. The patient lost her symptoms and seemed well. She has since been in college and has done heavy work; she had an operation for

appendicitis and is living a normal life. The neck is now normal and there are no symptoms. This is undoubtedly an exceptional case, for among a large number of this group of cases this is the only one that seemed to require other than medical care. Most of these patients acquire a normal thyroid after the menstrual periods are fully established. On account of this it is extremely difficult to estimate the real value of any treatment which may be instituted.

Group 3. Those patients having an enlarged thyroid with a definite hyperthyroidism active or at times potential. The enlargement may be due to a hyperplasia of a parenchymatous type (true Graves's disease), or it may be a colloid goitre, a cyst, an adenoma or any combination of these conditions. This is a group of patients in which the course of treatment is occasionally extremely difficult to decide upon. It depends largely upon the stage of the disease or condition present at the very time the patient is seeking advice. Two principles must be kept in mind: (1) Any pathology of the thyroid should receive the same prompt consideration as similar pathology does elsewhere in the body. If the indications are for surgery it should be undertaken; if for roentgen rays the same obtains. More will be said of this when discussing group four. (2) Due regard must be given to the stage, or degree, of secretion of the thyroid gland, determined by its effect upon the general health of the patient, before deciding upon any course of treatment. In toxic goitres of extreme degree and in true exophthalmic goitres medical treatment may be the only safe treatment at first, and may be a necessary preliminary to later surgical or roentgen-ray treatment. If, after a successful course of medical treatment, the thyroid gland still presents such pathology as would ordinarily require surgical interference, surgery should be undertaken promptly, *before there is a recurrence of disturbed function.*

In certain cases the intoxication may have reached such a stage that medical treatment, *i. e.*, physical and mental rest, abundance of food, support of the circulation and nerve sedatives, however carefully prescribed, will not bring about such amelioration as to make an operation a safe procedure. Under such circumstances it may still be safe to use roentgen-ray treatment, either as a preliminary to operation or without any thought of a subsequent operation. In these cases roentgen-ray treatment has been most satisfactory. In several cases where it was begun only as a preliminary treatment the results were so satisfactory that it was continued until the symptoms subsided and the swelling practically disappeared. Of course, there are occasionally fulminating cases which run a rapid course and for which no treatment, however carefully planned, is of any avail. One such case seen some years ago was most remarkable. The patient was a child's nurse. She had charge of two children in a family. Both contracted scarlet fever and died violent deaths within a week on account of kidney

complications associated with uremic convulsions. The nurse, who was very much attached to the children, harbored the idea that she was directly responsible for bringing about the contagion. She could not be convinced to the contrary and brooded continually. She had previously been perfectly well. Her pulse became rapid, the thyroid gland enlarged, the eyes protruded and tremor developed. The diagnosis was evident. Notwithstanding every care she became delirious, later comatose and died. The whole course of the disease was run in just two weeks. It will be seen that in group 3 the success of any treatment is largely dependent upon the proper selection of cases. The problem is practically the same as it is in gastric and duodenal ulcer. There are some patients who will get well with medical treatment and remain permanently well, while there are conditions in others which will interfere with recovery until surgery is undertaken, or roentgen rays are applied, and finally there are those who will not recover with any treatment. These are the fulminating cases, or the neglected chronic cases with definite vascular or nervous disturbances.

Group 4. Those patients having definite pathology of the thyroid, enlargement without any disturbances of thyroid function. This group includes malignant tumors, such as carcinomata, also the so-called "simple" goitres, or colloid growths, as well as the adenomata and cysts, and inflammatory reactions due to tubercular, luetic or other infections. They really have no disturbance of internal secretion, but may be potential cases. These are imperatively surgical conditions, especially when malignant or when producing pressure symptoms interfering with breathing or swallowing. Certain of these conditions, such as the adenomata and colloid goitres, yield satisfactorily to roentgen-ray treatment, which under certain circumstances may be preferable, but in emergency surgery is imperative.

By following such a grouping of patients as just described I have been able to advise more definitely as to the line of procedure in disease of the thyroid gland. There are, of course, border-line cases, but this occurs in any classification.

The first group includes strictly medical cases; the second group may need nothing but prophylactic care and extremely careful medication; when they need more they are already in the third group; the third group may be medical for a time and later surgical or roentgen ray or both; the fourth group is surgical always, but may present an enticing field for roentgen-ray investigation.

The physician who has only one treatment, be it medical, surgical or roentgen ray, either sees only one class of cases or fails to recognize a large class which might be successfully treated otherwise. While I would prefer to have the surgeon and the roentgenologist settle their own differences, if there are any, on this question, as an internist I feel it my duty to express an opinion. The internist usually

sees the cases first, no difference what stage of the disease may be presented. If medical treatment is not indicated, or if medical treatment has failed, or under certain circumstances if it has succeeded, he should be immediately in touch with the surgeon or the roentgenologist, or both. If he is as familiar with his case as he should be, he will go into such a consultation with pretty definite convictions. From my own experience I would say as between surgery and roentgen ray, that the former has a far larger field of application, and in skilful hands is comparatively safe. It has the added advantage of furnishing definite information, in that the tissue removed may be studied and the nature of the pathology determined. This is of the utmost importance for the future conduct of the case. The roentgenologist is necessarily frequently not altogether sure of the condition with which he is dealing.

The results of operative treatment are sometimes immediate, so that the patient is able in a short time to return to his usual life or occupation. On the other hand, the roentgen-ray treatment presents some advantages which cannot be passed by and which appeal to one very strongly. It is comparatively without danger: it leaves no scar; it is painless and gives very little inconvenience; if it is unsuccessful, surgery may be undertaken with possibly less risk.¹⁴

The absolute safety of the procedure may be questioned. May it not be possible by roentgen ray to destroy the function of the gland entirely, as happens in the radiation of the ovaries, and produce a myxedema? The surgeon from the time he entered this field has been reminded of the dangers of removing too much glandular substance, and there are records of unfortunate results. What assurance has the roentgenologist that he may not have similar experiences? These are some of the questions which concern the internist especially.

In conclusion the following summary might be offered:

1. Exophthalmic goitre, or hyperthyroidism from other causes, should be recognized early and treated promptly, on lines specified.
2. The earlier it is recognized the more likely medical treatment will be sufficient and give permanent results.
3. The neglected cases, or the cases having definite pathology besides, are likely to require surgery or roentgen ray, or both. In this is included treatment with radium.
4. The roentgen-ray treatment of the enlarged thyroid presents most attractive advantages, but the indications for its use do not seem so definite yet, and the results are not so certain.
5. In hyperthyroidism the roentgenologist and the surgeon at best can only break through a vicious circle for which the internist may or may not have been responsible.

¹⁴ Malcolm Seymour: The advantages of Roentgen-ray Treatment, Boston Med. and Surg. Jour., 1916, clxxv, 568.

HUMAN ARTERIOSCLEROSIS: SOME REMARKS CONCERNING ITS ETIOLOGY AND SYMPTOMATOLOGY.

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ETIOLOGY. Arteriosclerosis is another term for aging. It means that the vascular domain, especially the arterial portion, and also other tissue cells, are wearing out. There are some factors which we feel certain, and others which we suspect, speed up this aging process, yet in most instances we do not know the exact *modus operandi*. Among the factors which play an active part we find (1) the wear and tear of life, (2) infectious processes, (3) intoxications, (4) mechanical strain. The relative importance of these factors doubtless varies in individual cases, as does their relative importance, in the opinion of many observers who have given thought to the subject.

1. *The Wear and Tear of Life*. It is easy to grasp what is meant by this title. It is very difficult, if not impossible, in the present state of our knowledge, to accurately explain the concrete sequence of causes and events.

Our first thought, perhaps, suggests heredity. We know that certain organisms and machines are more enduring than others; more capable of adjustment to surrounding circumstances and more resistant to certain types of strain. But, unfortunately, we often cannot assign the reason, nor do we know the exact nature of the strain. The influence of heredity is quite as impossible to explain as is growth and longevity in different species of animals. Why does the swan live so much longer than the sparrow or the elephant than the mouse? Why do some individuals live to a ripe old age, having passed through hardships, physical strain, infectious disease, exogenous intoxications and severe trauma, while others succumb early and easily?

Oliver Wendell Holmes on being asked how a man should proceed in order to live to the age of seventy years, replied that he should pick his ancestors for one hundred years before he was born.

It is easy to show by mathematical formula the enormous and increasing strain to which the heart and arteries are subjected. Also that these strains may be and often are much enhanced by habits of life, such as severe muscular effort, and by causes such as chronic arterial hypertension. But, again, this leads us once more into the maze. Why the difference in individuals?

Some things, however, it appears do exercise profound effects. It is agreed that the modern high-tension life, kept under the spur

by ambition and competition, with inadequate mental relaxation and with insufficient physical exercise, which helps to redistribute blood and relieve congested vascular areas, does much to produce arteriosclerotic changes.

2. *Infectious Diseases.* It has been said, with truth, that "Venus loves the arteries." One of the definite advances of our knowledge within recent years has been the frequency with which syphilis produces disease of the aorta. It appears that although the involvement of this vessel is a frequent if not constant, as well as an early lesion, its symptoms rarely manifest themselves with obtrusiveness for sixteen years. As an illustration of this the army experience may be quoted. Out of 1,000,000 men examined 11,562 were rejected for cardiovascular diseases, and among these only 20 men were found to have aortic aneurysm; even aortic insufficiency of luetic origin was not common. With syphilis as a known, important factor of arterial disease, and with the current estimate that about 15 per cent. of our population has been thus infected, many cases of arteriosclerosis are accounted for. Other infections, such as typhoid fever and tuberculosis, may also be held accountable for some cases. In addition to the clinical evidence, aortic atheroma has been produced by the experimental injection of various pathogenic bacteria in animals. Focal infections doubtless also play a role.

3. *Intoxications.* Lead, alcohol and tobacco are regarded as potent factors. In regard to the former there can be no question. Lead may act (a) directly upon the bloodvessels or indirectly through the production of (b) nephritis and (c) gout. The role of alcohol is more in doubt, and difficult to evaluate, owing to the coincident presence of other causes. As an important etiological factor alcohol *per se* has certainly lost caste in recent years. Perhaps our great national experiment may in the future throw light on this subject. Tobacco establishes a far better claim as a noxious agent than alcohol. Experimentally the injection of nicotin in small quantities increases the secretion of epinephrin. Arterial lesions are readily produced by the injection of nicotin, and blood-pressure changes can easily be demonstrated in human beings. In a certain type of arteriosclerosis, thrombo-angiitis obliterans, a Jewish heredity, and the cigarette have been especially incriminated. And yet when one considers the number of heavy users of tobacco who live to old age, one wonders how great a role tobacco plays.

4. *Mechanical Factors.* Arterial hypertension, often associated with nephritis, justly receives credit for many cases of arteriosclerosis. This may be more or less localized, as in the aorta and brachial arteries of the laborer, or in the cerebral sclerosis of the man who works with his brain. As a rule, however, the process is more generalized, although the heart or the brain may be the chief point

of attack. As Osler has said, "The tragedies of life are largely arterial."

5. *Chemical Factors.* The whole trend of modern medicine is toward chemistry. Is it not natural to turn to chemistry as an explanation of our riddle?

(a) *Auto-Intoxication.* Metchnikoff's conception of arteriosclerosis as a result of "auto-intoxication," due to production and absorption of poisonous products, putrefactive in character and arising from the intestinal flora, has attracted much attention. While the possibility of this hypothesis in some cases cannot be denied it certainly has not been proved to be a constant or even frequent factor.

(b) *Internal Secretions.* Attempts have been made to show that arterial hypertension and vascular disease may result from disturbance of the internal secretions. We know that the medullary part of the adrenal gland and the infundibular portion of the pituitary are potent vasoconstrictors. Arterial lesions are readily produced experimentally by the injection of epinephrin, although they differ in type from human arteriosclerosis. Much stress has been laid upon epinephrin as a factor in the causation of arteriosclerosis, it being believed that it acts chiefly by its effect on the vasa vasorum. Contraction or occlusion of these vessels would naturally impair the nutrition and resistance of the arteries. In some clinical cases of arteriosclerosis, disease of the vasa vasorum is the only change demonstrable. Such lesions may produce both intimal and medial necrosis. (Cowan.) Degenerative disease of the adrenal glands, as seen in Addison's disease, is associated with hypotension; but this line of reasoning apparently leads us astray, since the adrenal glands are, it appears, only emergency organs which are not concerned in the normal maintenance of blood-pressure, and an increased epinephrinemia cannot be shown to exist in chronic hypertensive disease. It is possible, of course, that an individual living under continued high tension, with periods of excitement and strain, may suffer some arterial damage from this cause, but that it is much of a factor cannot be maintained.

Again, the secretion of the thyroid gland exerts a marked influence upon the circulation, greatly increasing the work of the heart, the rate of blood flow and dilating the peripheral vessels. Arterial thickening is a pronounced feature in long-standing cases, as is also cardiac hypertrophy. It has been suggested that an excessive protein diet acts through its effect upon the thyroid gland. It being pointed out that the plethoric gourmand presents many symptoms similar to those of hyperthyroidism, such as flushing, a sensation of warmth, palpitation, nervous irritability, increased blood-pressure, etc. (Sajous.) There also appears to be an interrelation between the ovaries and other glands of internal secretion. Vasomotor disturbances are common at the time of the menopause,

and arterial hypertension is often first manifested at this time. These and many other thoughts along this line are suggestive and interesting, but largely speculative and not explanatory of the basic cause of arteriosclerosis.

(c) *Protein Metabolism.* If then the chemistry which we speak of as endocrinology fails to solve the riddle of arteriosclerosis, can we turn to a more fruitful field, that of metabolic chemistry? In this domain we are equally at a loss for an answer. It is probable that certain products resulting from the digestion of protein or the products of metabolic activity—protein catabolism—may exercise deleterious effects upon the vascular system, but experimentally the products of hydrolysis and amine formation from protein are dilators of vascular structures. As an example, histidin, one of the common amino-acids, may be mentioned. Of course, it does not follow that only vasoconstrictors can produce arterial damage. Arterial lesions can be produced experimentally by the injection of toxins or epinephrin even if a rise of blood-pressure is prevented by the simultaneous injection of the nitrites. Clinically, it seems established that overindulgence in food, especially protein food, has deleterious results. Certainly, the withdrawal of proteins and the restriction of food generally to the point at which only the nutritive needs are supplied is often followed by a great ameliorization, if not an actual disappearance, of hypertensive symptoms.

SYMPTOMATOLOGY.

Bearing in mind the fact that arteriosclerosis is a general disease affecting not only the circulatory system, but probably also other tissues as well, it is not surprising to find that its symptoms may be practically coextensive with the ailments which flesh is heir to. It is equally obvious, inasmuch as arteriosclerosis is a normal biological development, which may begin at any age, that the early manifestations may be slight, vague, ill-defined and difficult to evaluate.

Many cases diagnosticated as indigestion, biliousness, neuralgia, neurasthenia, asthma, bronchitis are in reality the early manifestations of arterial disease. It is well to be skeptical regarding what appear to be purely functional derangements without demonstrable cause in individuals past middle life. It was doubtless with this or a kindred thought in mind that the following advice was offered by an experienced practitioner: "When the patient complains of his stomach, examine the heart; when he complains of his heart, examine the stomach." It is hardly necessary to recall the number of sudden deaths attributed to "acute indigestion."

It would profit but little to enumerate *in extenso* all the different symptoms which arteriosclerosis may occasion, but a few phases may perhaps merit allusion.

As is well known, sclerosis of the arteries is nearly always general, yet in a given case certain organs or systems are the chief sufferers. It is customary, therefore, to class the cases as (1) cardiac, (2) renal, (3) cerebral, (4) peripheral, (5) abdominal, (6) nervous. In each instance symptoms may arise as a result of spasm, diminution in caliber, thrombosis or rupture of a given vessel. Such symptoms are usually but not always brought on when an extra demand for blood, either locally or in other areas of the body, exists. Thus in the cardiac type one has as subgroups those in which (*a*) myocardial, (*b*) valvular and (*c*) coronary lesions and symptoms predominate the picture. In the renal group one finds (*a*) cases associated with the contracted kidney and often with very marked secondary vascular changes resulting from toxemia and hypertension, and (*b*) those cases which show the true red, beefy sclerotic kidney and often exhibiting few if any urinary symptoms. In the cerebral type one finds not only a loss of mental elasticity, an inability to concentrate attention or to enjoy things that once made an appeal; but also psychasthenic manifestations, vagaries of conduct or outbursts of excitement in people who had previously steered a straight course and kept an even keel. One also encounters amnesias and temporary failure, either partial or complete, of vision, hearing or consciousness; also aphasias.

The peripheral type is chiefly exemplified by vascular spasm, intermittent claudication, spontaneous cramps, neuritic pain as in erythromelalgia, localized gangrene, etc.

We must speak with less assurance regarding the abdominal type. Most often one sees flatulent indigestion simulating cholelithiasis or ulcer. The latter may actually exist as a result of localized endarteritis. A special type of angina, angina abdominis, has been described.

Finally, in the nervous group one finds vertigo and even convulsions epileptiform in character. Such convulsions occurring in individuals past middle life, in the absence of syphilis, lead and uremia, usually have an arteriosclerotic basis.

Arteriosclerosis may occur in infants, and when one takes the trouble to look for it, it is not infrequently found in young adults who may at the time show no vascular symptoms. The symptoms in these cases usually do not appear until arterial hypertension becomes an added factor, and this, in many instances, may be years after the peripheral arteries first show definite thickening.

But according to the modern conception, as has already been stated, arteriosclerosis is a general disease; general, not only in its arterial distribution but also in the fact that all the tissues of the body may show the effects of the disease even independently of the disturbances which result from a diminished blood supply. In other words, the chemical changes which cause vascular disease affect other tissue cells directly, just as they do the arterial walls.

Hence much attention has been focussed upon a so-called "pre-sclerotic" stage. Only after this stage has advanced will one be able to demonstrate arterial changes. Still later, as the case progresses, definite evidences of circulatory, renal or cerebral failure, or a terminal infection, will appear upon the scene. In the first stage various and often ill-defined phenomena make their appearance.

The earliest stage is always difficult, sometimes impossible of recognition. Generally, one notes what appear to be a beginning loss of bodily vigor, resistance to strain, or to infection, either with or without what appear to be slight functional derangements, involving the digestive, circulatory, renal or nervous systems. Sometimes the only noticeable changes are those of the skin, which becomes dry, wrinkled and atonic, with a diminished sebaceous activity, a tendency to chap, and suggests a possible hypothyroidism. Or perhaps the patient may simply show an apparently causeless anemia.

There is in the minds of many much confusion between arterial hypertension and arteriosclerosis. Indeed, the terms are unfortunately sometimes used interchangeably. Of course, the two conditions are often simultaneously present and prolonged hypertension often leads to arteriosclerosis. But that the reverse is true appears more than doubtful. (1) To begin with we are confronted with the great senile group whose arteries may be like pipe-stems but whose pressures are practically normal; (2) we have the large group of hypertensive cases in whom the increased pressure begins in middle life, is maintained at a very high level and precedes by many years the appearance of demonstrable arterial thickening; (3) it is not conceivable that a splanchnic vascular spasm can be maintained over months and years of life, especially without producing more local intra-abdominal disturbances than is the case, to say nothing of the fact that splanchnic sclerosis is but rarely demonstrable at autopsy.

In conclusion, it seems that clinical arteriosclerosis may simply be an involutional process, a part and parcel of aging; or it may be mechanical or toxic in origin. Just how this involutional process is brought about we are not in a position to state. But it seems more than likely that it will ultimately be shown to be the result of chemical changes associated with the bodily metabolism, which exert their effects upon the individual visceral, vascular and somatic cells, either directly or through the mediation of the ductless glands.

ARTERIOSCLEROSIS IN WILD ANIMALS.¹

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THE study reported here is a part of a general scheme of the Laboratory of Comparative Pathology at the Philadelphia Zoölogical Garden to place on record a review of the lesions found among the animals at the autopsy table, thus attempting to fulfil the objects of the collection, so aptly put in a quotation from Bacon's "New Atlantis," that we have upon our walls: "We have also parks and enclosures of all sorts, of beasts and birds, which we use not only for views and rareness, but likewise for dissections and trials, that thereby we may take light what may be wrought upon the body of man." The subject of vascular disease was taken up as the first step in a study of the cardiorenal system and has led to some interesting observations. The morbid processes covered in this report include only those described in human pathology today as productive endarteritis and degenerative arteritis or arteriosclerosis; it will be called angeitis as a collective term. Among the animals domesticated by man these lesions have received scanty attention, possibly because their association with other lesions is not pronounced, but mostly because they are relatively rare. An accepted standard text-book, Hutyrá and Marek, treats the subject casually, laying greater stress upon the varieties caused by parasites, while Zinslerling questions whether arteriosclerosis, like that seen in the human being, ever occurs in the horse. Another author has observed it in heavily worked draught horses. Arteriosclerosis has also been seen in dogs, and Kollisch states that the essential pathology is the same. The incidence among domesticated animals, as a whole, is not available, but it must be low. However, the occurrence of angeitis among wild animals is likewise not great, for we present the result of an analysis of 5464 autopsies, among which only 86 cases were discovered, that is about 1.5 per cent. The distribution of these cases is as follows:

Mammals autopsied, 1806; angeitis, 33 or 1.8 per cent.; birds autopsied, 3571; angeitis, 53 or 1.4 per cent.; all others autopsied, 87; angeitis, 0.

Before going on with the consideration of the features of these groups and lesions, it might be well to consider for a space a few general facts concerning the similarities and differences among man, lower mammals and birds. In so far as the gross anatomy of mam-

¹ This is a preliminary report upon the subject, the first step in the larger field of cardio-vasculo-renal pathology. It was read before the College of Physicians, Philadelphia, February 4, 1920.

mals as a class is concerned there are relatively few differences, the cardiovascular structures being built upon the same general plan and the physiology being very similar. The minute structure is likewise much of the same kind, the elastic tissues being, however, rather more abundant in the lowest mammals. The physiology of birds, however, must be constructed on a somewhat different plan, because their anatomy is quite different and their habits require a mechanism to control the distribution of strain on the cardiopulmonary system. As a class birds are, per size, oversupplied with heart and vessels, especially the trident-like group of arteries at the base of the heart. This may be in the nature of a reservoir or as a part of the pressure-regulating mechanism. The heart and the origin of the three great vessels lie more free in the thorax, and they lack the support of the well-organized mediastinal tissue seen in mammalia. Great air sacs communicating with the lungs and bones, surround this central system, which must therefore require adjustment when the birds fly high and low, dive or rise. These air sacs are present also in the abdomen and pelvis. I am unaware of any studies showing the operation of this mechanism or the seat of its control, and mention is only made to show that instead of a tissue pressure of more or less stability, as in mammals, there is a variable air-pressure in Aves. The physiological circulation of the blood, while subject, of course, to anatomical variations, is really much the same as in mammals. Microscopically a difference exists in the walls of the bloodvessels, fibro-elastic tissue being more prominent than in mammals, apparently at the expense of muscle fibers; perhaps upon this may depend some of the pathological differences. Birds have a temperature considerably higher than mammals, in some genera rising as high as 112° F.; a few genera seem to be poikilothermous. There is nothing at hand to show that the cardiovascular control is otherwise than is known for the human being. The hypophysis, adrenal and thyroid, by some thought to be essential to control of the vessels, are larger on the average in animals whose habits demand severe or prolonged muscular effort. For this statement I have no measurements or weights, but it is a matter of daily observation at autopsies on cats, dogs, eagles on the one hand, and lemures, rodents and parrots on the other hand. In the bird the adrenal cortex is distributed with nervous tissue through the body, the medulla being bare as a yellowish-brown mass, lying at the upper pole of the kidney beside the sexual organ.

If to these anatomical differences between mammals and birds and the variations of habits and habitats among both classes one adds the element of captivity, it will be at once apparent there is a very great number of variables, so great that one hesitates to draw conclusions. All that can be done is to point out certain more or less obvious groups of facts, in hope that other later observations will piece them all together.

The effects of captivity, including unnatural food and the absence of the chase, are very difficult to evaluate. While every attempt is made at the Garden to approximate natural food, it is obvious that this must be incomplete and that gastro-intestinal pathology is inevitable. As a matter of fact it is the most important factor to be dealt with in zoölogical collections. The question of senility, natural and induced by captivity, has been mentioned in several connections with animal pathology, but its effect is as yet unsettled.

The division into proliferative and degenerative angeitis may be open to some objection, but as the etiology of neither condition is settled, it is fair to consider under the former those changes which carry out the picture of the thrombo-angeitis proliferans or endoarteritis obliterans. It happens that in our study five instances were discovered affecting vessels in or near frank inflammatory processes. The animals affected with this productive process were three birds, a rodent and an elephant. In the case of two birds and the rodent the process was associated with chronic intestinal lesions, while in the elephant it was found as an endarteritis obliterans in large vessels of the lung of chronic pulmonary tuberculosis occurring in this animal.

Degenerative angeitis, arteriosclerosis, was observed in thirty-one mammals, the orders Primates, Carnivora, Marsupialia and Ungulata being represented, while Rodentia, Lemures and Chiroptera, of which we have many protocols, are missing; four of eleven orders are affected. The lesions take the form of roughened, rather opaque, intimal changes, with degenerations of the media, but there is usually missing that well-outlined, heaped-up, ulcerating, roughened intima so characteristic of late human atheroma and present to a slight extent in the Aves. One occasionally sees fatty yellow streaks in the lining, but they seem not to go on to calcification. The aorta is by far the most affected vessel, the lesions being usually present at the top of the arch and in the thoracic portion. There is one case among mammals and one in birds with the longitudinal ridging and opacity, but not the scarring, of syphilitic aortitis. Deformity is never great and aneurysms occurred only four times. Two instances of small sacculations in the aorta were found, a sort of Mönckeberg sclerosis; once also this occurred in a bird; these have not been cut to confirm the type names. Among the thirty-one cases ten show frank chronic renal disease, about equally divided between the degenerative and glomerular types. Six animals had myocarditis of fibroid nature, one, a monkey, showing distinct coronary sclerosis and concentric hypertrophy.

This type of arterial disease seems to affect a larger percentage of orders among the class Aves, twelve of seventeen being represented. Fifty-one instances of degenerative arteritis are recorded, and of these, birds of prey, parrots, ducks and geese supply twenty-seven; ostriches and storks and gallinaceous birds, however, are well represented.

The birds of prey are divided into Falconidæ (hawks, eagles) and Catharidæ (condors, vultures). The former are aggressive, the latter timid, usually getting what is left after the former have finished, although accused by some observers of preferring spoiled meat; the two groups eat the same things at the Garden. They supply 39 per cent. of the cases among the Aves and 19 per cent. of the total reported. The lesions, while most prominent in the aorta, are found also in main branches and take the form of heaped-up, irregular, yellowish-gray intimal patches over degenerative media; the superficial deformity may be marked at times, but little scarring occurs. Calcification has not been seen, but certain patches are quite like those of the human lesions.

Parrots present exceptions to the general picture in birds, for their lesions are more common in the smaller vessels and strongly resemble senile arteriosclerosis, with its medial degeneration and calcification, as seen in man. Perhaps a considerable number of our specimens have been pets for a time, thus subjected to the effects of civilization. These birds are known to be long-lived, perhaps up to a century, and the process may be a real senile arteriocapillary fibrosis.

Gallinaceous birds, chiefly grain-eaters, show insular atheroma in sharply outlined areas, as do the larger aquatic birds, storks, herons and the like. The anserine birds vary very much in the type of lesions, as indeed they do in habits and habitat, but the larger ones, like geese, show quite clearly a patchy intimal overgrowth and fatty deposit with less evident mesial change.

Renal lesions of a chronic nature were apparent in seventeen of the fifty-one birds, very uniformly distributed in percentage among the various avian orders. Nephritis in birds is not yet well enough known to determine exactly all the varieties, but the degenerative type seems more prominent, glomerular forms being, however, clear at times. Ten birds showed chronic myocarditis. Three aneurysms were found, two in geese and one in a vulture. In two of the eagle family a definite cardiac hypertrophy was noted, one in association with myocarditis and nephritis.

In only two cases of the whole eighty-six was chronic valvulitis noted, the aortic and mitral being involved, but the notes do not attempt to estimate the hypertrophy. A word might be added concerning the occurrence of fatty deposits in the intima without evidences of sclerotic change. This lesion occurs commonly in the human being, not infrequently appearing in young persons, with and without acute infectious disease and without apparent reason for chronic vascular degeneration. Such a fatty deposition is exceedingly rare in wild animals, and, when it occurs, is more patchy than in human beings. It seems to be connected with infection.

Our study tends to confirm the general opinion of the rarity of arteriosclerosis in the lower animals, but perhaps a closer study will

reveal more cases, especially since we know the groups in which it appears. It is most common in cats and dogs, bovines, predatory birds, parrots, gallinaceous and aquatic birds, and in these groups it is most definitely developed in those living on a protein diet. The lesion is very common in the orders showing the greatest number of cases of gastro-enteritis; this is especially true of parrots, aquatic birds and herbivorous and carnivorous mammals. The aorta is more affected in mammals, the disease is more distributed in birds. A rough similarity to the human aortic lesions is to be seen in the predatory birds and some of the carnivora, while the parrots exhibit degenerations in middle-sized vessels not unlike those of arterio-capillary fibrosis.

The animals most affected are those prepared by nature for severe or prolonged physical effort, such as in fight and flight. Aneurysms occur rarely, usually at points of branching and always near atheromatous plates; they are small and seem to retain part of all coats of the vessels, seldom becoming large enough to form their wall from the surrounding areolar tissue. More males than females are listed in the series, but as we have many more males on record, perhaps the difference would be less marked if the figures were closely comparable.

TWO CASES OF FIBRINOUS BRONCHITIS, WITH A REVIEW OF THE LITERATURE.

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DURING the past four and a half years, in which an intensive study on bronchial asthma has been made, the sputum of asthmatic patients has been carefully examined. As a result of careful examination of the sputum 2 cases of fibrinous bronchitis were noted. Although the history which the patient gives, and to a less extent the observation of the patient during an attack suggests the diagnosis, it is the finding of long, branching casts in the sputum that establishes the diagnosis of fibrinous bronchitis.

At various intervals all cases of fibrinous bronchitis, also known as plastic bronchitis and bronchitis pseudomembranosa, have been collected from the literature, but the best, most complete and most recent review of the literature and discussion of the disease was published by Bettman¹ in 1902. Previous to 1869, because of incomplete observations, it is difficult to say just how many cases of fibrinous bronchitis actually occurred in the literature, but a safe

estimation would put the total at about thirty. The interval between 1869 and 1902 covered by Bettman's paper furnishes about 50 cases; for a list of these cases reference may be made to Bettman's article.¹ From 1902 to 1920 I was able to find 31 cases in the literature: 2 of acute fibrinous bronchitis and 29 of the chronic variety. Those cases reported in the literature since Bettman's paper will be listed at the end of this paper.

That the condition is an unusual one is evidenced by the small number of cases reported in the literature; however, the condition is not rare, since the author has learned of local cases that were never reported and of 2 other cases, observed by Dr. Lawrason Brown,² that may yet be reported, and, furthermore, while reading the literature, the author ran across several instances in which cases were shown and demonstrated before local foreign medical societies; but since these were never published as cases they are not indexed in the literature on the subject. A more careful examination of the sputum of patients with bronchitis, asthmatic bronchitis and the like would probably result in a still greater yield of cases of fibrinous bronchitis.

Cases of fibrinous bronchitis fall naturally into three groups, namely, acute bronchitis with expectoration of branching casts, chronic bronchitis with expectoration of branching casts and cases in which branching casts were not expectorated but were found in the bronchi at autopsy. Since the chief distinction between the acute and the chronic form is the duration of the disease or the repetition of attacks in the latter, and since most acute cases become chronic because death or permanent relief rarely follows one attack, and since the symptomatology is the same in both types, this paper will discuss only the chronic type of fibrinous bronchitis.

Branching casts may be found in the sputum of diseases other than fibrinous bronchitis. Occasionally in organic heart disease, in pulmonary tuberculosis, in pneumonia and frequently in cases secondary to diphtheritic inflammation of the larynx, branching casts are expectorated. Furthermore, it is not uncommon to find small casts without branchings in the sputum of asthmatic bronchitis, and rarely these are found in association with pulmonary edema and lobar pneumonia. None of these conditions, however, are considered to be fibrinous bronchitis, since the formation of casts is secondary or related to some other condition. In other words fibrinous bronchitis is idiopathic, whereas in the condition just mentioned above the formation of casts is symptomatic.

A brief analysis of the symptomatology as usually obtained from cases of fibrinous bronchitis is as follows: The usual age of onset is between the ages of thirty and sixty, with a progressive increase of incidence up to middle life and then a gradual decline. Occupation, family history and chemical irritants seem to have little or no bearing on the disease. Often there is a previous history of some

acute infectious disease, and almost invariably there is a past history of chronic bronchitis. The onset of chronic fibrinous bronchitis is usually with an exacerbation of a chronic catarrhal condition; there may be some fever. In the acute cases there is usually a preceding acute bronchitis, accompanied by considerable elevation of temperature and frequent chills. In both the acute and chronic forms there are paroxysmal attacks of dyspnea and some cough, and these generally immediately precede the expectoration of casts. The dyspnea is chiefly inspiratory in type, the cough is very hard and there is considerable cyanosis and frequently a feeling of tightness or constriction in the chest. Symptoms are temporarily relieved by the expectoration of casts, and the severity of the symptoms are greatly out of proportion to the size or number of casts which, when raised, relieve the attack. Between the raising of large casts, small and incomplete portions of casts are usually expectorated. The amount of respiratory distress would seem to be out of proportion to the degree of limited obstruction caused by the small incomplete casts unless there is a reflex obstruction involving a larger area of the bronchial tree. Hemoptysis is rare. There may be considerable loss of weight and strength.

Physical signs do not distinguish fibrinous bronchitis from ordinary bronchitis, with the exception that when the casts are *in situ* a very coarse, dry, clicking sound, probably caused by the flapping to and fro of loosened portions of casts, may be heard with both inspiration and expiration. Impairment of resonance may be elicited and all types of rales may be heard. One would expect impairment or absence of breath and voice sounds in the area of lung that is obstructed, but this is rarely the case, probably because there is not total obstruction by the casts, which usually have a lumen.

For a detailed description of the casts reference should be made to Bettman's¹ paper. In general the large casts average 10 cm. in length and show branchings down to the seventh degree. They are white in color and have a consistency of fibrin. Many branches have little intumescencia, which may be due to air bubbles or to diverticuli. A lumen may extend throughout the branches, but often the terminal branches end either as a solid plug or as a Curschmann's spiral. Usually small portions of casts are expectorated for some time after a large cast has been expelled. Microscopically the casts usually present a fibrillar, stratified ground substance containing in its meshes leukocytes. The amount of fibrin varies and there is not as much present as one would anticipate. In each case reported only one or two distinct types of bacteria have been found, so that each author has considered that the bacteria found in his particular case were the cause of the condition. On reviewing the literature, however, the bacteria found in the different cases vary so widely that one must conclude either that any type of

organism may cause the condition or that the organisms present in the casts bear no relation to the cause of the disease.

There seem to be no definite sequelæ or complications in this disease, and only rarely is there a fatal termination as a direct result.

CASE REPORT. F. W. P., white, male, aged fifty-five years, was under observation at the Peter Bent Brigham Hospital (Med. No. 22065) from September 22 to September 27, 1919.

The patient complained of cough at night. His parents died of old age and his sisters are well. There is no history of illness or death in the immediate family and no family history of constitutional diseases. The patient has been a farmer all his life and he has always lived in Massachusetts. His past history follows: He had chicken-pox, measles, mumps and whooping-cough in childhood, scarlet fever at the age of six, and six years ago for one year he had rheumatism, swelling and redness of the joints of his fingers and toes, but this did not prevent him from working. He has had a right inguinal hernia for eight years. He has been subject to occasional colds, with some expectoration. Recently he has had nasal obstruction, which was relieved by removal of polypi. He has had no cardiorespiratory, gastro-intestinal, genito-urinary or neuromuscular symptoms. There has been no loss of weight.

The patient's present illness began five months ago, following removal of nasal polypi. Ever since their removal he has had coughing spells of two or three hours' duration almost every night. He is free from these coughing spells during the daytime, and if he sleeps sitting up the cough is much less severe. The paroxysms of coughing are followed by dyspnea of a few minutes' duration. Previous to the cough there is little or no dyspnea, but during the attack both inspiration and expiration are labored. No cyanosis has been noted. At the beginning of an attack he raises frothy sputum, then it becomes slimy, and toward the end of the attack he raises twisted white or yellow strings. There is also a white, watery discharge from the nose during the paroxysm. There is no history of hemoptysis, night-sweats or loss of weight.

Physical examination reveals nothing abnormal as regards the skull, scalp, hair, face, eyes, ears, nose, gums, tongue, pharynx, larynx or neck. He is well developed, thin but not emaciated; his mouth is negative except for a slightly offensive breath, and his teeth are negative, with the exception that there are many fillings and two are missing.

The thoracic cage is small in size and the manubrium is very prominent (chicken-breasted). Chest expansion is good and equal on the two sides; rate and depth of respiration are normal. Examination of lungs reveal no abnormalities, with the exception that a few transient, low-pitched, coarse, bubbling rales are heard, after violent coughing, over the larger bronchi in front on both sides of

the sternum. Examination of the heart, bloodvessels, abdomen, genitalia, rectum, lymphatic glands, bones, skin and extremities reveals nothing abnormal. The systolic blood-pressure is 124 and the diastolic is 80.

Examination of urine, stool and blood revealed nothing abnormal; no eosinophilia. Blood-serum Wassermann reaction was negative.

Roentgen rays showed no abnormality in the sinuses, no pus pockets about the teeth, and the heart to be normal but ptotic in type. The diaphragm was within normal limits; there was diffuse peribronchial thickening throughout both chests; the right apex showed slight mottling and the left hilus showed a slightly increased density.

During the patient's stay of six days in the hospital he slept propped up in bed in order to prevent severe coughing spells. On several occasions, however, about midnight the patient had attacks of difficult breathing, lasting about an hour. Epinephrin injected subcutaneously in 0.5 c.c. doses would give moderate relief; sterile water injected subcutaneously had no effect. The patient's temperature on two occasions was 99°, otherwise it was normal; his pulse ranged from 70 to 90 and respirations varied between 20 and 25 per minute. He had no severe coughing spells while in the hospital, but every day he did raise long branching segments of casts from the smaller bronchi. About ten days previous to entrance to the hospital he had had a severe attack of cough and dyspnea, and at this time he expectorated a large cast.

Examination of the sputum revealed a rather thick, tenacious, slimy material, in which casts and plugs were suspended. The casts were 2 to 5 cm. in length, averaged from 2 to 4 mm. in diameter, had a lumen with various intumescencia and 2 to 4 branches. The plugs were solid molds of the smaller bronchi and some ended in Curschmann's spirals. No tubercle bacilli were found in the sputum; there were a large number of eosinophils present and a few Charcot-Leyden crystals.

Microscopic examination of the casts revealed a fibrillar, stratified, ground substance; the ground substance was mucus and the fibrillar structure was fibrin in the meshes, of which there were polymorphonuclear leukocytes and eosinophils. The solid plugs on section showed a matrix with strings of mucus and fibrin infiltrated with small lymphocytes and polymorphonuclear leukocytes. No tubercle bacilli or influenza bacilla were found either in the casts or in the plugs; many cocci were present.

Bacteriological examination of the sputum alone revealed hemolytic streptococcus subacidus and non-hemolytic streptococcus ignavus; from the casts alone hemolytic streptococcus subacidus and non-hemolytic streptococcus salivarius were recovered. In obtaining these types of bacteria a portion of the sputum was washed and shaken in dextrose bouillon, and then blood-agar plates were poured;

the casts were teased out, washed in sterile saline, shaken and macerated in dextrose bouillon from which blood-agar plates were poured. Smears of the macerated casts and plugs revealed no tubercle bacilli and no influenza bacilli; only cocci in chains were seen.

The second case will not be given in detail, since it has already been published by Dr. Henry A. Christian³ in the *Medical Clinics of North America*, Boston number, 1919, II, 1255. A summary of this case follows:

D. R., white, male, aged twenty-two years, a plumber's helper by occupation, entered the Peter Bent Brigham Hospital (Medical No. 9990) complaining of breathlessness. His family history, past history, and habits are unimportant. There is no history of exposure to irritating fumes.

The present illness began suddenly three months ago in September, 1918. He was awakened by a severe cough, a feeling of breathlessness and oppression. After an hour the attack gradually passed and he went to sleep. Each night since he has had similar attacks which have increased in frequency, duration and severity. Cough always precedes the attack and the raising of thick, stringy sputum relieves the attack. During the attack expiration is easy, but inspiration is difficult; there is considerable wheezing and cyanosis and a feeling of tightness in his chest. During the day he has mild attacks directly after eating. Epinephrin relieves the attacks. In November, 1919, two months after the first attack, many polypi were removed from his nose without apparent benefit. He has lost forty pounds in weight.

Physical examination is negative, with the exception that examination of the lungs reveals a slightly hyperresonant note throughout; expiration is distinctly prolonged and slightly high pitched and a few scattered crepitant rales are heard throughout the lungs.

Roentgen rays showed that the entire right chest was less radiant than the left and a diffuse peribronchial thickening which is more marked on the right side and dense glands at both lung roots.

The patient was under observation twenty-four days. During this time his temperature usually varied between normal and 99°, with an occasional swing to 100°; his pulse varied between 80 and 100 and his respirations were usually 20 per minute, with an occasional increase to 30 per minute. Every night he had an attack of coughing, dyspnea, chiefly inspiratory, wheezing and expectoration of branching casts. Mild attacks occurred during the day. Epinephrin relieved the attacks. Administration of potassium iodide and an autogenous sputum vaccine seemed to be of no benefit. His blood constantly showed a slight polymorphonuclear leukocytosis.

Repeated examination of the sputum revealed many branching casts, many eosinophils and Gram-positive cocci in chains. No tubercle bacilli were found. A hemolytic and a non-hemolytic

streptococcus in about equal numbers were obtained by plating the sputum in blood agar. Sections of the casts revealed chiefly mucus, with a fibrin reticulum in the meshes of which there were large numbers of mononuclear eosinophils and streptococci.

Discussion of the Etiology of Fibrinous Bronchitis. The etiology of this disease is obscure. In a few cases at postmortem there was a break in the continuity of the bronchial epithelium, in others the bronchial epithelium has contained a large number of mucus-secreting cells which would suggest an exaggerated secretion from the normal mucus glands. The fact that the casts are composed in greater part of mucus would substantiate the increased secretion of mucus and the small amount of fibrin in the casts might come from the rupture or break in the bronchial epithelium. Retention of this mucus and fibrin in the bronchial tree for some time would permit of coagulation or hardening of these substances so that a cast is formed. There would be some irritation causing the accumulation of leukocytes, and since bacteria are normally present in the bronchi, leukocytes and bacteria would naturally be present in the casts.

Since in some cases of fibrinous bronchitis there is an element of neurosis, this condition has been considered by some as allied to mucous colitis. These two conditions are similar in that the intestinal casts of mucous colitis resemble closely the bronchial casts of fibrinous bronchitis, and the etiology of both conditions is obscure.

The author prefers to correlate fibrinous bronchitis with asthmatic bronchitis, bronchiectasis and chronic bronchitis. In almost all of the cases of fibrinous bronchitis, asthmatic bronchitis and bronchiectasis there is a preceding history of bronchitis, and throughout the course of these diseases there is a background of bronchitis. When patients with bronchitis develop paroxysms of dyspnea and suffocation the condition is then called asthma; in order to distinguish this condition from true bronchial asthma the author calls this condition asthmatic bronchitis. For the author's differentiation between true bronchial asthma and atypical or asthmatic bronchitis one may refer to the *Oxford Medicine* by Christian and MacKenzie.⁴ If in cases of bronchitis, breaks in the bronchial epithelium, with more or less loss of it occur, fibrinous bronchitis may result; if these breaks invade the deeper structure of the bronchial tubes, thereby causing a weakening of the structure, bronchiectasis may result. In asthmatic bronchitis there is a simple catarrhal desquamation of the bronchial mucus membranes much in excess of that which occurs in bronchitis, and in fibrinous bronchitis there is a permanent loss of the epithelium. Furthermore, in asthmatic bronchitis it is not uncommon to find non-branching casts and plugs in the sputum. Very likely all of these conditions are caused by bacteria, and we know that a large proportion of the cases of bronchitis and asthmatic

bronchitis are due to bacteria, since autogenous sputum vaccines frequently relieve the condition; in fibrinous bronchitis and bronchiectasis, however, vaccines do not benefit, because too much destruction of tissue has taken place. Local lack of vitality probably explains why bacteria produce these conditions in some individuals. Because of the local lack of vitality or inadequate resistance of the bronchi to infection in some persons, bacteria, which in others are non-pathogenic, are able to set up infectious processes. Flurin⁵ speaks of the "syndrome de débilité bronchique," which is characterized by hyperesthesia of the mucosa, unstable local circulation and special secretory response to any causes liable to stimulate secretion in the mucous glands.

Conclusions. Cases of fibrinous bronchitis would probably not be as rare as the literature would indicate if the sputa of patients were more carefully examined.

The diagnosis of fibrinous bronchitis is made only by the finding of long, branching bronchial casts in the sputum of cases that do not have tuberculosis, diphtheria, pneumonia or some other primary bronchial disease.

Fibrinous bronchitis is an idiopathic disease, the cause of which is unknown. Although it may be due to a neurosis it seems more closely allied to bronchitis, bronchiectasis and asthmatic bronchitis.

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CURVES OF SUGAR AND UREA AFTER STANDARD PROTEIN MEALS.

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ONE of the writers¹ previously reported observations of the effects of diet on the blood sugar of normal persons and diabetics. The results showed no demonstrable influence of protein in the type of cases studied. Rolly and Oppermann² observed a rise of blood sugar after protein meals in some diabetics. Strouse, Stein and Wisely³ found no evidence of a rise of blood sugar in normal persons after carbohydrate-free meals. In animals with suitably severe diabetes controlled by undernutrition, Allen⁴ has regularly found marked hyperglycemic curves following protein ingestion. Mosen-thal, Clausen and Hiller⁵ found that carbohydrate-free meals cause no hyperglycemia in non-diabetics or in some diabetics, but in other diabetics they produce more or less rise of blood sugar. This rise was found particularly in cases with initially low blood sugars, and was commonly missed in cases with marked hyperglycemia at the outset. The rise of blood urea after protein ingestion in rela-

¹ Jacobsen, A. Th. B.: *Biochem. Ztschr.*, 1913, lvi, 471-494.

² *Biochem. Ztschr.*, xlix, 1913, 278-292.

³ *Bull. Johns Hopkins Hospital*, xxvi, 1915, 211-215.

⁴ *AM. JOUR. MED. SC.*, 1917, p. 153, Chart VIII.

⁵ *Arch. Int. Med.*, xxi, 1918, 93-108.

TABLE I.—50 GM. PROTEIN TEST IN FIVE NORMAL PERSONS.

	¹ Mr. H. E., 22 years.				² Dr. S., 29 years.				³ Dr. J., 34 years.				⁴ Miss M., 28 years.		⁵ Mr. C., 22 years.	
	Blood.		Urine.		Blood.		Urine.		Blood urea, mgm. per 100 c.c.		Urine.		Blood urea, mgm. per 100 c.c.		Urine.	
	Plasma sugar, per cent.	Urea, mgm. per 100 c.c.	Urea, gm. per cent.	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Urea, mgm. per 100 c.c.	Urea, gm. per cent.	Urea, mgm. per 100 c.c.	Urea, per cent.	Urea, gm.	Urea, per cent.	Urea, gm.	Urea, per cent.	Urea, gm.	Urea, per cent.	Urea, gm.
Before	0.106	20.0	2.63	..	0.110	13.5	1.71	..	24.2	2.42	15.0	46.4	2.39	..
2 hours	0.100	21.9	1.81	1.46	0.125	18.3	1.30	1.69	..	2.13	2.13	2.13	20.5	42.1
4 hours	0.114	28.0	2.16	1.49	0.115	19.4	1.39	2.26	28.0	2.29	2.68	2.68	..	44.2	2.74	6.44
6 hours	0.105	28.0	2.38	1.45	0.115	22.6	0.64	2.18	32.6	1.75	1.96	1.96	31.4	46.4
8 hours	26.0	17.2	0.56	1.81	28.4	1.82	1.86	1.86	..	46.4	3.83	6.05
24 hours	18.0	1.02	10.62	..	20.5	1.14	6.65	22.2	1.25	10.00	10.00	17.2	38.8	2.80	13.55
Urea excreted in 24 hours (gms.)	15.04	14.16	18.65	18.65	26.05

tion either to retention or metabolic variations has been investigated, especially by Addis and Watanabe.⁶ An investigation was therefore undertaken to determine the curve of plasma sugar in normal, diabetic and nephritic individuals after standard protein meals and was extended to cover the urea of blood and urine.

METHODS. The standard procedure was that the subjects voided urine and were bled, then ate a breakfast consisting solely of 50 gm. protein in the form of beefsteak, and 200 c.c. water. Two patients in the series received only 40 gm. protein. Every two hours thereafter urine was passed and blood taken and 200 c.c. water drunk. After eight hours a very light supper was taken of cornstarch and candy with a trifle of fruit, having negligible protein content. Water was then taken at will, but no other food until after the blood and urine samples the next morning, which closed the twenty-four-hour period. Sugar was determined according to Benedict, urea by the urease method of Van Slyke and Cullen and total nitrogen by the usual Kjeldahl method. Blood sugars were determined in two of the normal individuals, in confirmation of the writer's previous work regarding the negative effect of protein. The sugar changes were within the limits of accidental fluctuation.

There was a very appreciable rise of the blood urea during the eight-hour experimental period, followed by a fall at the end of the twenty-four hours in every individual except No. 5. This person was a technician in the laboratory. His urine, like that of all the others in this group, was free from albumin and casts. He was supposedly in perfect health, though subject to occasional headaches. It was learned that he had by chance eaten excessive quantities of meat on the day before the test. These facts explain the exceptionally high excretion and the lower blood urea after twenty-four hours. In a strict sense this person probably has a slight nephritis, and he has been advised to follow a fairly low protein diet. Irrespective of this question it is evident that the initial percentage of blood urea is not a safe criterion of the tendency to rise after a certain protein intake.

TABLE II.—PROTEIN TESTS IN SEVEN DIABETICS.

1.—28 years.

	(40 gm. protein.) Blood.		
	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Chlorides, mgm. per 100 c.c.
Before	20.0	0.139	568
1 hour	24.0	0.174	518
2 hours	26.0	0.174	576
4 hours	32.2	0.158	576
6 hours	36.2	0.165	587
9 hours	35.2	0.123	572
24 hours	29.0	0.122	

Excreted 11.6 grams total nitrogen.

⁶ Arch. Int. Med., 1917, xix, 507-517.

2.—27 years.

	Blood.			Urine.		
	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Chlorides, mgm. per 100 c.c.	Vol., c.c.	Sugar.	Acetone.
Before	47.2	0.043	526	..	0	0
1 hour	53.4	0.070	557		0	0
2 hours	60.4	0.068	504	85	0	0
4 hours	74.6	0.064	527	290	0	0
6 hours	76.6	0.050	546	240	0	0
9 hours	58.4	0.043	521	290	0	0
24 hours	54.4	0.040	..	1700	0	0

Excreted 14.2 grams total nitrogen.

3.—35 years.

	Blood.			Urine.		
	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Chlorides, mgm. per 100 c.c.	Vol., c.c.	Sugar.	Acetone.
Before	0.074	587			
1 hour	40.0	0.110	584	260	0	0
3 hours	42.0	0.144	590	145	0	Slight
5 hours	0.139	555	115	0	Mod.
7 hours	44.0	0.136	590	125	0	Faint
9 hours	56.0	0.091	587	130	0	0
24 hours	50.4	0.048	561			

Blood.

	4.—64 years.	
	Plasma sugar, per cent.	Urea, mgm. per 100 c.c.
Before	0.176	24.0
2 hours	0.197	26.0
4 hours	0.205	30.0
6 hours	0.205	34.2
24 hours	0.242	39.2

5.—43 years.

	Plasma sugar, per cent.
Before	0.130
5 minutes after	0.130
1 hour after	0.144
2 hours	0.181
3½ hours	0.192
4½ hours	0.208
5½ hours	0.203
6 hours	0.203

6.—31 years.

	Blood.			Urine.				
	Urea mgm. per 100 c.c.	Plasma sugar per cent.	CO ₂ vol. per cent.	Vol. c.c.	Urea per cent.	Urea gm.	Sugar.	Acetone.
Before	31.4	0.091	61.4	..	1.79	..	0	0
2 hours	35.8	0.135	68.1	87	2.23	1.96	0	0
4 hours	46.4	0.147	62.5	113	2.24	2.55	0	0
6 hours	46.4	0.132	57.8	103	2.80	2.89	0	0
8 hours	46.4	0.125	70.0	100	—	—	—	—
24 hours	34.6	0.150	—	1020	1.49	15.21	0	0

Excreted 22.6 grams urea and 14.5 grams total nitrogen.

7.—27 years.

	October 26.						November 20.									
	Blood.			Urine.			Blood.			Urine.						
	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Chlorides, mgm. per 100 c.c.	CO ₂ vol. per cent.	Vol. c.c.	Urea, per cent.	Urea, gm.	Sugar, per cent.	Nitro-prusside.	Urea, mgm. per 100 c.c.	Plasma sugar, per cent.	Vol. c.c.	Urea, per cent.	Urea, gm.	Sugar, per cent.	Nitro-prusside.
Before	14.8	0.314	582	51.0	..	1.38	..	4.8	Heavy	11.8	0.194	—	0.46	..	0	0
2 hours	17.8	0.341	566	45.3	185	1.23	2.27	5.5	"	14.0	0.191					
4 hours	18.8	0.341	558	40.4	200	1.01	2.02	5.5	"	20.5	0.272	258	1.02	2.64	0	0
6 hours	16.6	0.319	566	43.3	248	1.36	3.36	3.66	"	24.7						
8 hours	17.8	0.280	574	..	225	1.23	2.76	2.0	"	21.6	..	190	1.78	3.39	0	0
24 hours	9.0	—	—	47.1	1780	0.59	10.50	0.65	"	20.5	0.269	—	0.87	..	0	0

Excreted 20.9 gm. urea. (Total excretion lost.)

The diabetics were mostly young, but were all alike in having the severe form of the disorder, more or less completely under control by undernutrition treatment. There was a history of three to ten years' duration and an advanced degree of emaciation and weakness in all except No. 1, who had apparently been diabetic less than six months and was only slightly thin. The preceding diets ranged from fasting, in the case of the first test on patient No. 7, up to 60 gm. protein, 20 gm. carbohydrate and 1000 calories in patient No. 3. All were free from albuminuria or casts except No. 2. There was moderate edema in No. 2 and slight in No. 6 at the time of the test. Patient No. 3 had formerly been subject to edema, but was free at this time. The others had never exhibited edema. The plasma chlorides remained within normal limits in all determinations. The blood-pressure was normal or subnormal in all.

The general program of the tests was the same as above described, except that after the initial period of eight or nine hours a supper of negligible food value was given, consisting of bran biscuits, agar jelly, one dish of thrice-cooked vegetable, and coffee or infusion of cocoa shells. Certain points concerning the results in individual patients may be noted as follows:

Patient No. 1, starting with a normal blood urea of 20 mgm. per 100 c.c., showed a greater rise than any of the normal subjects, viz., to 36.2 mgm. at the sixth hour. The plasma sugar, starting with a slight hyperglycemia of 0.139 per cent., jumped to its maximum of 0.174 per cent. in one hour, and in general fell after the second hour. Undernutrition on this day is indicated by the plasma sugar, lower after twenty-four hours than at the outset, and by the excretion of nitrogen exceeding the intake. This absence of retention is of interest in connection with the prolonged rise of blood urea.

Patient No. 2 was admitted with a history not only of the severest type of diabetes but also of several mild attacks of renal colic followed by passage of small calculi, with blood in the urine at these times and pus afterward. In the hospital the albumin in his urine frequently gave Esbach readings as high as 1.5; the sediment showed enormous numbers of pus cells but no casts. Later attacks caused his blood urea to rise above 130 mgm. per 100 c.c., and at the time of the test he may be considered as representing a combination of diabetes and nephritis. Starting at 47.2 mgm. per 100 c.c., the blood urea rose to its maximum of 76.6 mgm. at the sixth hour. At the same time the twenty-four-hour nitrogen output was nearly double the intake, in correspondence with the very low diet in a patient possessing a minimum of body fat. In the days preceding the test, the rather rapid fall of the formerly intractable blood sugar to a subnormal level was another indication of danger. Under these circumstances, though the diabetes was the most desperately severe of the series, the rise of the plasma sugar from the ingestion

of protein was considerable in proportion to the original amount but trivial in absolute figures. The patient is still alive after nine months, free from glycosuria and acidosis and much improved in strength, and at home with normal plasma sugar.

Patient No. 3, with a somewhat less degree of diabetes and under-nutrition, started with plasma sugar of 0.074 per cent., and reached the maximum of 0.144 per cent. in three hours after eating. Thereafter the curve progressively fell. The urea analysis before eating was lost. From 40 mgm. per 100 c.c. one hour after eating, it rose to 56 mgm. at the ninth hour. The lack of parallelism with the sugar curve is especially noticeable. During digestion a well-marked acetone reaction developed in the urine and later disappeared, due either to the protein or to the trifle of fat in the lean meat.

Patient No. 4 was tested when the diabetes was only partially under control, as indicated by the hyperglycemia of 0.176 per cent. This rose to its maximum of 0.205 per cent. at the fourth and sixth hours after eating and traces of sugar were excreted. The urea curve was parallel, starting at 24 mgm. per 100 c.c. and reaching 34.2 mgm. at the sixth hour. The morning figures of 0.242 per cent. plasma sugar and 39.2 mgm. urea proved that the patient broke diet in the evening.

Patient No. 5 had an unusually intractable diabetes for his age, and the question arose whether his slow progress was due to breaking diet or whether his hyperglycemia could actually be due to the small quantities of prescribed food. He was accordingly given the 50 gm. protein test while under constant observation in the laboratory, and the blood followed for sugar alone for six hours. The marked hyperglycemia demonstrated the true severity of the condition, and subsequent acquaintance with the patient and the ultimate favorable outcome confirmed his fidelity.

Patient No. 6 underwent fasting immediately upon admission and was given the test with 50 gm. protein as soon as the plasma sugar became normal. The plasma sugar rose to a maximum of 0.147 per cent. at the fourth hour, but was still 0.15 per cent. the next morning, indicating that the patient could not yet tolerate this quantity of protein without hyperglycemia. For this reason the protein ration for the ensuing days was set at 30 gm. During digestion the CO_2 capacity of the plasma showed some of the familiar digestive variations. The blood urea rose from 31.4 mgm. per 100 c.c. to 46.4 mgm. at the fourth hour and held this maximum for at least four hours. The two-hour urinalyses showed no retention as compared with normal persons in Table I and the total twenty-four-hour excretion was excessive, as is natural for the emaciated organism under these conditions. No acetonuria appeared during the test.

Patient No. 7 was subjected to two tests, the first during active

glycosuria before treatment, the second during the early stage of treatment, when there was hyperglycemia but no glycosuria.

In the first test on October 26 the variations in blood urea and sugar were slight and parallel for the first eight hours. This test represented a partial fast following abruptly upon the former mixed diet; therefore the result at the end of eight hours was a slight fall in blood sugar. The blood urea, on the contrary, was a trifle higher than at the first, but after twenty-four hours had fallen to the markedly low level of 9 mgm. The urea excretion was high, both for the twenty-four-hour and for the two-hour periods. The plasma bicarbonate fell distinctly during this protein test and the urinary nitroprusside reaction remained heavy. At the same time the urinary sugar fell.

By November 20 the patient had reached a point where sugar and nitroprusside reactions were constantly negative in the urine and the plasma bicarbonate normal, but hyperglycemia persisted. The blood urea started at 11.8 mgm. per 100 c.c., reached a maximum of 24.7 mgm. at the sixth hour and was still up to 20.5 mg. the next morning. The plasma sugar was 0.194 per cent. before eating, practically the same two hours after, but at the fourth hour was found to be 0.272 per cent. and was still 0.269 per cent. the next morning. The reason for the elevation of both urea and sugar here after 50 gm. protein probably is that the preceding diet had contained only 30 gm. protein. The quantitative twenty-four-hour urine collection was spoiled by the patient's fault. Though this patient's phenolsulphonephthalein test had shown an elimination of 60 per cent. the first hour and 20 per cent. the second hour, and both the urea and chloride functions had likewise been found normal, the impermeability for sugar is indicated by the absence of glycosuria with the high plasma sugars mentioned.

The first three patients listed had typical hypertensive nephritis of severe grade, with only traces of albumin and rare casts. No. 1 had slight edema and ascites, due to myocarditis and cirrhosis of the liver. Nos. 2 and 3 were free from edema. Case No. 4 was of the "parenchymatous" type, with normal or subnormal blood-pressures, extremely heavy albumin and much edema. All had been for some time preceding on diets liberal in calories but containing only 30 or 40 gm. protein. The program of the test days was as described for normal subjects. The liberal supply of water of these days was a sharp departure from the usual regimen of these patients, who had been on diets poor in both salt and fluid, and instead of sweeping out nitrogen it may have contributed to its retention.

All the tests were characterized by marked deficiency of the urea output as compared with normals, and especially in Case 1 this apparent retention was extreme. In all except Case 4 the urine volume indicated also a marked retention of fluid. The blood urea rose in all during the first eight hours, but this rise was nothing

TABLE III.—50 GM. PROTEIN TEST IN FOUR NEPHRITICS.

	1.—42 years.						2.—10 years.						3.—45 years.			4.—19 years.				
	Blood.			Urine.			Blood.			Urine.			Blood.			Urine.				
	Urea mgm. per 100 c.c.	Plasma sugar per cent.	Chlo- rides mgm. per 100 c.c.	Urea per cent.	Vol. c.c.	Chlo- rides per gm.	Urea mgm. per 100 c.c.	Plasma sugar per cent.	Chlo- rides per 100 c.c.	Urea per cent.	Vol. c.c.	Urea mgm. per 100 c.c.	Urea per gm.	Urea mgm. per 100 c.c.	Urea mgm. per 100 c.c.	Urea per cent.	Vol. c.c.	Urea mgm. per 100 c.c.	Urea per cent.	Vol. c.c.
Before	16.0	0.108	508	24.6	0.146	585	31.5	10.8
2 hrs.	19.0	0.133	498	0.49	21.5	0.05	26.0	0.158	585	0.71	..	40.6	34	0.36	12.9	35	0.83	2.92
4 hrs.	28.0	0.143	498	0.24	33.6	0.144	543	51	1.82	0.93	32.3	73	1.04	0.76	16.2	105	1.79	1.88
6 hrs.	34.6	0.132	480	..	57.0	0.51	40.0	0.136	620	35.7	62	1.03	0.61	16.2	125	1.49	1.86
8 hrs.	36.2	0.106	414	0.31	36.0	0.69	37.8	0.139	593	173	1.99	2.25	31.3	25	1.35	0.33	20.5	65	1.69	1.10
12 hrs.	30.1	..	462	0.24
24 hrs.	27.0	..	523	1.90	750	0.27	275	1.47	1.04	34.3	660	0.61	1.04	10.8	1110	0.47	6.64
Urea excreted in 24 hrs. gm.	2.46						7.23						6.15			11.79				

extraordinary as compared with the records of the normals and diabetics and failed totally to correspond to the comparative nitrogen elimination. In Case 1 the blood urea remained elevated at the end of twenty-four hours, as if indicating the nitrogen retention, but in Case 4 it ended at the same level where it began, and in Case 3 the elevation was trivial. Dilution probably played some part in maintaining the percentages at such levels; also, with the ample carbohydrate and calories of the usual diets, true storage as protein may have been a factor; but obviously much is unknown concerning the nitrogen retention of nephritis.

Patient No. 1 started with a normal plasma sugar of 0.108 per cent., which was moderately increased during the first six hours after eating. Patient No. 2 started with hyperglycemia of 0.146 per cent., which rose to 0.158 per cent. at the second hour, then gradually fell. Several previous writers have called attention to hyperglycemia in occasional cases of nephritis, especially with hypertension, and as such reports have been based on various methods of analysis, it is evident that the excess material present affects copper salts as well as picric acid, and may be glucose. But in view of the possible errors due to creatinin or similar substances it was deemed best to defer any conclusions concerning nephritic blood sugars until truer figures should be available by the use of the procedure recently proposed by Benedict⁷ for removal of the interfering material.⁸ One of us (J.) proposes to carry out further tests comparing the Benedict method with a copper reduction test for the blood sugar.

CONCLUSIONS. 1. After a standard meal of 50 gm. protein there is generally a rising curve of urea in the blood, which, as a rule, is higher in patients with severe diabetes or nephritis than in normal persons.

2. The blood-urea level is not a reliable index of nitrogen retention. In some instances, for example in diabetics, it may possibly bear some relation to the rate of protein catabolism. On the whole, it seems to be governed by so many factors of the previous diet, fluid retention and unknown metabolic conditions that by itself it forms an uncertain basis for conclusions.

3. The plasma sugar of normal persons is not appreciably altered by this quantity of protein.

4. The substances in nephritic blood, which react like sugar to the Benedict test, are increased after a protein meal.

5. A typical curve of hyperglycemia follows the ingestion of protein in suitably severe cases of diabetes. This is likely to be missed

⁷ Benedict, S. R.: Paper read before the Biochemical Society, Cincinnati, Ohio, December 30, 1919.

⁸ Subsequent analyses in this clinic with charcoal kindly provided by Dr. Benedict have shown no more than slight changes in the above curves. Therefore either the rise of plasma sugar after protein meals is not specific to diabetes or a diabetic tendency is thus demonstrable in some cases of nephritis.

if active symptoms of glycosuria or hyperglycemia are present, as the effect of 50 gm. protein could scarcely be expected to be noticeable amid such a surplus of sugar. Rarely also the rise may be slight in extreme exhaustion. Under the conditions of strict diet treatment this reaction to a standard protein meal may be used as a measure of the severity of diabetes and a guide both to the protein allowance and the total ration, and it has lately been used for these purposes in this clinic.

TREATMENT OF SURGICAL SHOCK IN THE ZONE OF THE ADVANCE.¹

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THE nature and treatment of shock has, in recent years, attracted considerable attention from the profession, especially on the part of the surgeon. War-time conditions naturally brought under observation greatly increased numbers of shock cases. The situation presented exceptional opportunities for the study of shock and it also demanded a plan for specialized treatment. This was all the more necessary when it became evident that in the advance zones the surgeons, when busy, were very busy, and had no time for carrying out specialized treatment. Internists, assisted and trained by physiologists, were therefore called in to help in what has generally been considered a strictly surgical problem. The plan devised by the medical department of the A. E. F. was to send into the advanced areas so-called "shock" teams, composed of medical officers (internists), nurses and corpsmen, especially trained and equipped for the treatment of shock. In preparation for the work the medical officers were given a special course in the nature and treatment of shock at the central medical laboratory at Dijon, under the supervision of Lieut.-Col. Walter B. Cannon, M.C., Boston, Mass.

In general the substance of the lectures and demonstrations given at Dijon may be summarized as follows:

I. THEORETICAL. Whether shock be due to hemorrhage, exposure to cold and wet, lack of food and drink, injury to muscle or nerve tissues, singly or in combination, it was agreed that in shock we find a condition of persistent low arterial blood-pressure, rapid pulse, pallor or slight cyanosis, sweating and rapid respiration, slight or

¹ The cases reported were observed by Shock Team No. 116, in charge of Captain George Strode, M.C. (Harrisburg, Pa.), and Shock Team No. 154, in charge of Captain W. R. Ohler, M.C., during the St. Mihiel and Argonne Meuse offensives. I wish to express my appreciation to Dr. Strode for permitting me to group all the cases together.

moderate acidosis. Owing to the conditions under which shock teams would have to work, blood-pressure determination was considered the best single method of determining the existence and the severity of shock. A systolic pressure of 100 was set as the minimum reading and members of shock teams were urged not to send a patient to the operating room with a pressure below 100 unless absolutely necessary.

II. OUTLINE OF TREATMENT. (a) Control restlessness by using morphin in comparatively large doses.

(b) Restore body heat by promptly warming the patient. The following methods were suggested and were found efficacious:

1. Hot-water Bottles (the army canteen makes an excellent hot-water bottle when the ordinary rubber one cannot be secured) placed between the feet, between the thighs, on the chest (hands folded over bottle) and in the axilla.

2. The Use of Hot Air. An efficient method in a field hospital is to place the litters on saw-horses, place one or two ordinary lanterns on the ground near the litter and close in the space by means of blankets draped from the litter to the ground. In an evacuation hospital other methods are generally available. We were able to secure small oil stoves and by means of ordinary stove pipe direct the warm air under a bed cradle covered with a blanket.

(c) Restore Body Fluids. 1. Force Fluids by Mouth: Hot soups, tea, coffee during first few hours. Warm soda bicarbonate drinks suggested in order to aid in overcoming condition of acidosis.

2. Fluids by Rectum. Especially indicated in severe shock or when the patient cannot take large amounts of fluid by mouth.

3. Intravenous Gum-salt Solution. In many cases of hemorrhage the infusion of certain fluids will restore the fluid bulk, and such a restoration of blood volume may be all that is needed to pull the patient through a critical period. Indications for giving gum salt are therefore the same as for giving intravenous normal saline solution. Gum-salt solution, so-called, is a 6 per cent. solution of gum acacia in normal saline. Theoretically it does not diffuse out of the vessels as rapidly as normal saline solution, and consequently gives a more lasting rise in blood-pressure.

4. Blood Transfusion. When considerable blood has been lost the reserve supply of body fluid may be so small that the tissues can give up very little fluid to the circulation. Moreover, in such instances, supplying additional oxygen as well as additional fluid is indicated. Blood transfusion presents the only means of increasing the oxygen-carrying elements of the blood.

The citrate method was adopted throughout the A. E. F. as being the most practicable of all methods. From 500 to 700 c.c. of blood was withdrawn from an arm vein of a donor directly into a bottle containing 2.1 grams sodium citrate in 100 c.c. normal saline. By taking care to have the stream of blood flowing freely and to keep

the receiving flasks rotating no coagulation resulted. The citrated blood was introduced through an arm vein of the recipient, pressure being exerted by using the bulb of a blood-pressure apparatus and forcing air into the flask. In cases of extreme shock when the blood-pressure was very low it often was necessary to cut down on the vein of the recipient. Type sera of Groups II and III were provided. Blood grouping was done according to the macroscopic method described by Vincent.² Members of shock teams were advised to keep a number of Group IV donors (so-called universal donors) on hand because of the saving of time in using only this particular group.

Approximately 125 cases of shock were observed during our service. In addition about 100 patients (postoperative cases) were sent to the shock ward who did not prove to be cases of shock, inasmuch as all had an entrance blood-pressure of 100 or more. It was the habit of members of surgical teams to send postoperative cases requiring special attention into the shock ward because such attention could not be given in the cold, busy, crowded general wards. It is quite possible that many of these cases were thus prevented from "going into shock." At any rate it was our feeling that the care of this type of case alone justified the work of a shock team.

In a study of the cases of actual shock an attempt has been made to group the cases according to the type of treatment as well as the severity of shock. Routine treatment consisted in rest, warmth, forced fluids (mouth and rectum), special treatment in intravenous gum-salt solution and blood transfusion. The severity of shock was determined by history, clinical appearance and blood-pressure readings. It was practically impossible to depend to any great extent upon history for determining the duration of shock. Wounded men very often could not tell just when they had been injured nor how long a time it took them to reach the evacuation hospital. The loss of all sense of time on the part of soldiers who took part in the terrible Argonne fighting was, in many instances, quite amazing. Moreover, there was no time to take a detailed history. It was our business to get the patients ready for operation just as quickly as possible. Only thus could infection be controlled and lives saved.

The fear of infection, therefore, as well as the degree of shock influenced us in the treatment. Thus many cases undoubtedly were given special treatment, when, had we been able to postpone operation, such treatment would have proved unnecessary. Whenever it was possible the effects of routine treatment were observed for a few hours before special treatment was given.

Group A. Forty-nine Preoperative Cases of Slight Shock.

² Jour. Am. Med. Assn., vol. lxx, p. 1219-1220.

Entrance blood-pressure varied from 60 to 100 systolic. Routine treatment (rest, warmth, forced fluids by mouth and rectum) was instituted. Three of the cases died from infection. All of the others responded promptly to the treatment as outlined, the blood-pressure rising to normal within two hours. All stood operation well and were eventually transferred from the shock ward in good condition.

Group B. Sixteen Cases of Extreme Shock. In every instance the patient's general condition and the meager history pointed to a condition of shock for a number of hours. The extremities were cold, skin clammy, pulse rapid, thready, in several instances not palpable; pallor was extreme; restlessness more or less marked; respiration rapid and shallow; temperature subnormal. Entrance blood-pressure averaged around 60 systolic, and in five cases could not be read at all. It was evident that all the patients had lost considerable blood, but no readings were made to determine the extent of hemorrhage.

In addition to routine treatment all the various forms of special treatment were tried on this group. Seven cases were treated with gum-salt solution alone. In each case 500 c.c. of the solution was given at once, followed in one instance by 500 c.c. more at the end of an hour, and in another instance by 800 c.c. normal saline solution. Five cases were treated with both gum-salt solution and citrated blood. About 500 c.c. of the gum salt given at once followed within one hour by from 400 to 700 c.c. of blood. Finally there were four cases in which blood transfusion alone was done. From 600 to 700 c.c. citrated blood was given within half an hour after admission.

None of the patients in this group responded in any way to the treatment given, and all died within three hours following admission.

Group C. In contrast with the above group, consider a group of 36 cases of moderate shock, with a blood-pressure of 80 or below, in which the treatment consisted of nothing but rest, warmth and fluid by mouth and rectum. None of these cases had lost much blood nor was there evidence of infection. Shock was probably due in a very large measure to cold, exposure, lack of food and fluids. In this group the following 2 cases seem worthy of special mention.

CASE I.—Gunshot wound of the abdomen, five days post-operative. The patient had been in the ambulance practically the entire day. Condition on entrance: cold; clammy; pulse thready; color good; systolic blood-pressure 60; diastolic not readable; temperature subnormal. Active measures were taken to warm the patient up, and within two hours after admission his blood-pressure rose to 110 and within twenty-four hours he was able to be transferred to another ward.

CASE II.—Gunshot wound of left arm, preoperative, fourteen hours in an ambulance. Condition on entrance: patient cold;

pulse thready, barely palpable; slight pallor. Patient had been wrapped in wet blankets, and his clothing also was wet. Entrance blood-pressure 60. Treatment consisted of warmth and forced fluids by mouth. Within two hours blood-pressure rose to 85 and in four hours to 90. Patient sent to operating room; amputation of the left arm; blood-pressure immediately after operation 90; within twelve hours 110. Within twenty-four hours patient was able to be transferred to another ward.

The average entrance systolic blood-pressure in the remaining cases of this group was between 70 and 75, and all responded very favorably within four to six hours.

Group D. A group of 24 cases of moderately severe shock. In this group all the forms of special treatment were tried in addition to the regular routine measures. This was done not because we made any particular attempt to experiment on manner of treatment but because the group, as a group, presented such a variety of problems. In order to call attention to these problems the cases will be subdivided into groups according to the type of treatment.

Subgroup 1. CASE I.—Gunshot wound of leg; extremities cold; pulse thready, rate 118; blood-pressure 90; 500 c.c. of gum-salt solution given, with rise in blood-pressure to 98 within one hour. Thigh amputation for beginning gas-bacillus infection. Returned to shock ward; blood-pressure 62; 500 c.c. gum salt solution given, followed by a rise in blood-pressure to 70 in four hours, 80 in seven hours, and 110 within about twenty hours. Patient receiving warm saline solution by rectum constantly. Patient transferred from shock ward in good condition.

CASE II.—Gunshot wound of right arm and shoulder; extremities cold; pulse 120, poor quality; blood-pressure 60 to 70; 500 c.c. of gum-salt solution given, with rise in blood-pressure to 80 within six hours; sent to operating room; shoulder amputation; returned to shock ward; blood-pressure 70; 500 c.c. of gum-salt solution given, followed by a gradual rise in blood-pressure, reading 110 within about twenty hours. Patient transferred from shock ward in good condition.

CASE III.—Gunshot wound of both legs; extremities slightly cold; pulse 90, fairly good quality; blood-pressure 88; 500 c.c. gum-salt given; rise in pressure within three hours to 98. Operation, extensive débridement of both legs; returned to shock ward with blood-pressure of 92, which gradually rose to 110 within twenty hours. Patient transferred from shock ward in good condition. Gum-salt solution apparently acted very well in tiding this patient over the operation. There was not much loss of blood, neither was there evidence of infection.

CASE IV.—Gunshot wound of legs; received in shock ward in apparently good condition; extremities warm; pulse 120; blood-pressure 110; patient seen by surgical chief, who decided that the

case was not urgent and could wait for operation. Patient sent to operating room fourteen hours after admission; blood-pressure had already fallen to about 95 and gas gangrene had begun. High amputation of left leg. Patient returned to shock ward; blood-pressure 90, which fell in two hours to 50; 500 c.c. of gum-salt solution given, followed by a rise in blood-pressure to 70 in two hours, with no further rise in four hours. Gas-bacillus infection apparent in other leg. Six hours after operation patient died.

CASE V.—A case in which it was felt at the time that gum-salt solution had perhaps done harm. A postoperative case, thigh amputation for beginning gas gangrene; admitted to the shock ward in apparently good condition, except that the blood-pressure was only 60. Within two hours the pressure rose to 88, but within four hours fell to 70. At this time 500 c.c. gum-salt solution given. The administration of the gum solution was followed by a severe chill and the patient died within two hours. This was the only case in which a severe chill followed the administration of gum-salt solution. It might well be argued in this case that the fluctuating blood-pressure was an evidence of severe infection, and that therefore the case was unsuitable for intravenous medication.

It will be noted in the above group of 5 cases that there was little or no hemorrhage. In Cases I, II and III gum-salt solution served well to tide the patient over the period of operation, even though in 2 of the cases there was some evidence of infection. Case IV is a case of severe infection and intravenous gum salt had little or no effect on the course of the disease. In Case V we are left in doubt as to whether or not gum-salt solution hastened death. In the opinion of the writer it did not, because there have been many instances in which rapidly spreading gas-bacillus infection has caused sudden death.

Subgroup 2. CASE I.—Gunshot wound of the abdomen; postoperative; considerable hemorrhage; pulse 164; blood-pressure 64; 500 c.c. of gum-salt solution given; fall in blood-pressure within three hours to 60; 200 c.c. of blood given followed by a rise in blood-pressure to 68 within six hours; 450 c.c. more of blood given followed by a slow but constant rise in pressure to normal. Constant rectal saline during first twelve hours. Patient was transferred from shock ward in good condition.

CASE II.—Gunshot wound of right arm. Postoperative; considerable hemorrhage on operating table. On admission to shock ward blood-pressure 50; pulse 130; skin warm; 500 c.c. gum-salt solution given within one hour of admission. Pressure down to 68 in one hour and fluctuated between 68 and 60 during the next two hours; 200 c.c. blood given, with a rise in pressure to 70 within two hours; 450 c.c. blood given, with a rise in pressure to 105 within four hours. Patient eventually transferred in good condition.

Shock in above two cases was due to hemorrhage. Gum-salt

solution apparently did little good, but, as a matter of fact, probably helped considerably to tide the patient over until a complete transfusion could be done. Case II illustrates the great value of the citrate method in war conditions; 600 c.c. of blood was drawn for this patient's first transfusion, but only 200 c.c. was given him because another admission to the ward seemed to be in greater need of the remaining 400 c.c. Later it was possible to secure another donor and complete the transfusion.

CASE III.—Gunshot wound of both legs; skin cold, moist; pulse thready; patient slightly restless; admission blood-pressure 74; 500 c.c. of gum-salt solution given; no change in blood-pressure in three hours; 500 c.c. more gum-salt solution given; blood-pressure rose in two hours to 85 but fell to 70 within four hours. Patient was then transfused with 300 c.c. of blood, and within twelve hours blood-pressure had risen to 110 and remained permanent. Patient developed gas gangrene in both legs, and both were amputated. Patient stood the operation well, but subsequently died of extensive gas infection.

CASE IV.—Gunshot wound of the tibia; postoperative; gas-bacillus infection; admitted in poor condition; blood-pressure 84; 500 c.c. gum-salt solution given; pressure fell in four hours to 68; 400 c.c. gum-salt solution given; pressure continued to fall to 60 in eight hours; 400 c.c. of blood given; pressure rose from 60 to 108 in eight hours. Constant rectal saline. Amputation of arm necessary for gas gangrene. Following operation blood-pressure 88; 500 c.c. of gum-salt solution given, followed by a rise in pressure to 100 in twelve hours. Patient died the next day from extensive gas infection.

CASE V.—Postoperative; leg amputation for gas gangrene; admitted in poor condition; blood-pressure 70; 500 c.c. of gum-salt solution given; fall in blood-pressure to 60 within three hours; 600 c.c. of blood given and pressure rose from 60 to 98 within eight hours, and then began to fall again, due to extensive bleeding from necrotic tissue in stump. 700 c.c. more blood given, but impossible to control hemorrhage, and the patient died.

CASE VI.—Gunshot wound of leg and buttock; postoperative for beginning gas-bacillus infection; blood-pressure 50; 500 c.c. of gum-salt solution given, with no response in three hours; 450 c.c. of blood given and pressure rose to 100 within twelve hours. Second operation necessary; amputation of leg and extensive débridement of buttock and other leg. Pressure fell to 84, rose in next two days to 110. Third operation necessary; further débridement of buttocks. Patient stood operation well; gas gangrene controlled; patient eventually evacuated in good condition. Patient on almost constant rectal saline during entire stay in shock ward.

CASE VII.—Postoperative. Amputation of right leg for gas-bacillus infection. Admission blood-pressure 80; pulse 104; skin

warm. Two hours after admission blood-pressure 75; 500 c.c. gum-salt solution given. No change in pressure for one and a half hours, when pressure fell to 50. Within an hour 600 c.c. citrated blood given; pressure began to rise at once and within four hours was 98. Patient was able to be transferred to another ward the following day, but subsequently died of infection.

Case VIII.—Gunshot wound of right thigh, with beginning gas infection; patient cold, pulseless; blood-pressure not readable; 500 c.c. of gum-salt solution given, with no results; 700 c.c. of blood given within an hour; pressure came back to 70 within four hours. Transfused a second time, with 700 c.c. of blood; pressure rose to 80 within two hours; sent to operating room; long anesthesia; patient died on the operating table.

Note that this patient was really in "shock" when sent to the operating room. It is probable that the patient's vasomotor apparatus was just able to maintain a pressure of 80, but the long anesthesia and the operation, together with a rapidly advancing infection, were more than the unstable circulation could stand.

The above subgroup of eight cases is noteworthy, because considerable hemorrhage or gas-bacillus infection or the combination was present in each case, and because special treatment in each case consisted of both intravenous gum-salt solution and blood transfusion. Mention has already been made of Cases I and II, where shock was due to hemorrhage and where infection was absent. Gum-salt solution did little good in these two cases because blood was the fluid needed and no intravenous solution can serve as a substitute for blood. In the remaining six cases severe gas-bacillus infection was present. Practically no response resulted from the administration of gum-salt solution in these cases. The response to blood was more encouraging, but eventually all the cases with one exception succumbed to the infection. This one case (VI) was remarkable, because an extensive gas-bacillus infection was eventually controlled. Note in this subgroup how the presence of infection complicates the results regardless of the form of treatment.

Subgroup 3. CASE I.—Gunshot wound of leg; beginning gas infection; pulse barely felt; extremities cold; blood-pressure 70; considerable loss of blood; 600 c.c. of blood transfused; pressure rose to 100 in four hours. Operation: amputation of left thigh; patient stood operation well; transferred in good condition, but subsequently died from gas infection.

CASE II.—Multiple wounds; beginning gas infection; extreme shock; pulseless; blood-pressure 70; 650 c.c. of blood given; pressure rose to 85 within three hours, during which time patient absorbed nearly two quarts of fluid by rectum. Operation: extensive débridement; following operation pressure fell to 50; 800 c.c. of saline solution given under the skin; pressure rose slightly; patient died before another blood transfusion could be done.

CASE III.—Gunshot wound of back; severe hemorrhage; extremities cold; pulse not palpable; blood-pressure 68; 700 c.c. of blood transfused, also 800 c.c. of saline solution given under the skin; pressure rose to 100 within ten hours, during which time patient absorbed three quarts of fluid by the rectum and one quart by mouth. Operation: extensive débridement. No evidence of infection. Patient stood operation well and was transferred improved.

The remaining cases of the group, IV, V, VI, VII, VIII, IX and X are here grouped together, because they are so similar to Case III, just mentioned. In none was there evidence of infection, and all had lost considerable blood. Blood-pressure, from 60 to 70. All responded very favorably to 700 c.c. of blood and all were transferred from the shock ward in good condition.

In subgroup 3 special treatment consisted of blood transfusion alone. In those cases in which shock was due to hemorrhage and in which there was no infection the response to blood was very prompt. In cases in which gas-bacillus infection was present the results were the same as in the other subgroups.

In Group D (subgroups 1, 2 and 3) cases of shock have been presented in which special treatment consisted of (1) gum-salt solution alone; (2) gum-salt solution followed by blood transfusion, and (3) blood transfusion alone. As a result of a study of these cases the following conclusions seem justified: (1) Gum-salt solution is of greatest service in cases of moderate shock when there has been little or no hemorrhage and when there is no severe infection. In cases of hemorrhage it may tide the patient over for a period, but it is not a substitute for blood. (2) Blood transfusion alone is indicated in all cases of severe hemorrhage. (3) In the presence of gas-bacillus infection neither gum-salt solution nor blood transfusion serves to halt the infection. Only the exceptional case gets well.

DISCUSSION. The importance of such simple procedures as body warmth, rest and forced fluids in the treatment of surgical shock has long been emphasized. Probably nowhere has there been better opportunity to note the good results from such treatment than in the war zone. Especially were we impressed with the way in which shock cases absorbed fluids. It was not at all unusual for a shock case to absorb four or five pints of warm saline by rectum in about an equal number of hours. Unfortunately it was impossible to keep an exact record of the fluids taken, nor was it possible to note the effect on hemoglobin. Clinically, however, we felt very strongly that the forcing of fluids either by mouth or rectum was a very important part of the treatment.

The question as to the value of intravenous gum-salt solution in the treatment of shock has been much discussed by the various workers in the A. E. F. Apparently results in general were disappointing. At first our feeling was in agreement with this opinion,

but a careful study of the cases cited does not justify this opinion. Just as there are a great many factors to be met in the problem of "shock," so all these factors must be brought out in the criticism of any given method of treatment. For the purposes of this discussion the most important considerations are (1) duration of the condition of "shock," (2) presence of infection, and (3) amount of hemorrhage.

It has often been noted that when patients have been in a condition of shock over a period of hours the organism fails to respond to any form of treatment. It would help in the problems here presented could we state definitely just how many hours each patient had been in "shock." This has not been possible. In Group I, however, we have a series of cases in which, as far as could be determined, the condition of shock had existed for a number of hours. As has been noted all forms of treatment failed in this group. It so happened that our first experiences with gum-salt solution were with patients of this group. Consequently, first impressions were far from encouraging.

The presence of infection, especially a rapid devitalizing infection like that of the gas-bacillus, greatly complicates the problem of the treatment of "shock." It will be noted in Group D that in a number of cases in which there was little response to gum-salt solution, gas-bacillus infection was present. It is true that better results were obtained in these cases when blood was also given, but even when transfusions were done the end-result was the same apart from exceptional cases. In fact, we fell into the habit of making a diagnosis of gas-bacillus infection when, for no other evident reason, the patient failed to respond properly to treatment. Gum-salt solution, therefore, cannot be condemned as an aid to treatment from the results in cases in which "shock" was complicated by gas-bacillus infection.

The most important single factor in the problem of "shock" is the question of hemorrhage, especially how much hemorrhage. In order to treat shock cases intelligently we ought to know when intravenous solutions are needed and when blood is needed. It is quite apparent that shock teams, as a rule, had no means of actually determining this fact. No intravenous solution will serve the purpose when the demand is for oxygen-carrying corpuscles. Theoretically, gum-salt solution will sustain the circulation better than normal saline solution, but gum-salt solution cannot serve as a substitute for blood. From our own experiences, and from conversations with members of other shock teams, it seems to the writer that gum-salt solution was often called upon to do just this thing.

It will be noted that those cases in which gum-salt solution did good were cases of moderate shock, with little or no hemorrhage, without gas-bacillus infection, and when the solution was given at the time of operation to tide the patients over a critical period.

No doubt if we had confined our use of gum-salt solution to this type of case, and especially to the period when the patient was on the operating table, our results would have been different. Whether or not normal saline solution would have served the purpose as well we are unable to say, since no comparisons were made in our series between normal saline solution and gum-salt solution.

Recently, Lee,³ Robertson and Bock⁴ have thrown light on the problem of when to give fluid and when to give blood, and have suggested methods of calculating total hemoglobin and blood volume. Unfortunately, we were not in a position to make these calculations until just before the Armistice, so have no figures to offer.

CONCLUSIONS. 1. The appointment of teams specially trained and equipped to treat cases of surgical shock was justified.

2. The importance of such routine procedure of treatment as rest, warmth, forced fluids by mouth and rectum is beyond question.

3. Intravenous gum-salt solution is not a substitute for blood. It has its greatest use in cases of moderate shock, with little or no hemorrhage and without gas-bacillus infection. In such cases the solution should be given just before or during operation, to tide a patient over a critical period.

4. In cases in which both blood volume and oxygen-carrying elements are needed, blood transfusion alone serves the purpose.

5. Intelligent treatment of shock can only be carried out when methods are at hand to determine when fluids are needed and when blood is needed.

6. In any criticism of methods of treatment of shock, the duration of shock, the presence of infection and the extent of hemorrhage must be considered.

7. The citrate method of blood transfusion is simple and gave uniformly good results.

HYPERGLYCEMIA IN ITS RELATION TO IMMUNITY.

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THAT the storage and mobilization of the carbohydrate molecule within the organism is a very delicately balanced condition is fairly

³ AM. JOUR. MED. SC., No. 4, vol. clviii, pp. 570-577. The case records mentioned by Lee as coming from our service are not included in this series.

⁴ Jour. Exper. Med., No. 2, vol. xxix, pp. 139-171.

well demonstrated by the recorded results of various investigations. It is known that sugar metabolism may be upset in one of two ways: One method, which produces what is probably a metabolic disturbance, was first described by Jacobsen,¹ who found a temporary hyperglycemia after the ingestion of considerable amounts of glucose. Jacobsen's method, more or less modified, has been used by many investigators² in studying various diseases. The results of these investigations may be summarized in the statement that hyperglycemia occurs in a number of different pathological conditions and that the type of reaction encountered is not specific for any given pathological condition.³

There exists another method, first recorded by Bloom,⁴ by which the carbohydrate metabolism may be upset, namely, the injection of adrenalin. Adrenalin is not the only substance which upon injection is capable of inducing hyperglycemia; thus peptone⁵ and various salts,⁶ as well as some of the products of protein decomposition,⁷ have been shown to possess the same power. The delicacy of the hyperglycemic reaction to adrenalin has been emphasized by Underhill and his co-workers, who showed that it could be accentuated or diminished by various substances. The administration of anesthetics, the physical changes undergone by the aviator and the injection of at least one mineral acid have also been described as causing a temporary increase in the blood sugar. A reaction induced, as is hyperglycemia, by so many different agents must of necessity play a most important part in the physiological and pathological processes of the organism.

One of the commonly offered explanations of the hyperglycemic reaction is that the sugar metabolism is controlled by the glands of internal secretion, and that as these are stimulated or depressed, increases or decreases in blood sugar occur. A further investigation of this explanation forms the subject of our first experiment, in which the attempt was made to simulate the condition of temporary overactivity of one or another of the endocrine glands by the subcutaneous injection of gland extracts.

Rats were used for the experiment. They were fasted for 12 hours; a blood-sugar determination was then made and followed directly by subcutaneous injection of one of the various gland extracts. Exactly 45 minutes after the injection and again 120 minutes after the injection blood-sugar estimations were repeated.

¹ *Biochem. Ztschr.*, 1913, lvi, 471.

² Williams and Humphreys: *Arch. Int. Med.*, 1919, xxiii, 537. Hamman and Hirschman: *Ibid.*, 1917, xx, 761. Hopkins: *AM. JOUR. MED. SC.*, 1915, cxlix, 254. Taylor and Hutton: *Jour. Biol. Chem.*, 1916, xxv, 173. Janney and Isaacson: *Arch. Int. Med.*, 1918, xxii, 160.

³ Rohdenburg, Bernard and Krehbiel: *AM. JOUR. MED. SC.*, April, 1920.

⁴ *Deutsch. Arch. f. klin. Med.*, 1901, lxxi, 146.

⁵ Kuriyama: *Jour. Biol. Chem.*, 1917, xxix, 127, 139.

⁶ Underhill et al.: *Jour. Biol. Chem.*, 1908, iv, 395; 1916, xxv, 461, 467; 1905-06, i, 113; 1911, ix, 13; 1911-12, x, 159; 1914, xix, 119; 1917, xxix, 127.

⁷ Watanabe: *Jour. Biol. Chem.*, 1918, xxxiv, 73.

The blood was obtained from the tail vein and the sugar content estimated according to the Epstein⁸ method.

While the Epstein method may be objected to on the ground that it is not very accurate, it can also be maintained that, whatever the error may be, it is the same in each test, and since our results are not based upon the accuracy of determinations of small fluctuations, but are wholly relative, the error can be disregarded when repeated estimations seem well correlated. However, care must be taken that the same pipette and graduated tube are used at all three estimations with any given animal, for it has been our experience that variations of from 25 to 30 per cent. are not infrequent as between two different pipettes or graduated tubes. Neglect of this factor would, of course, introduce a grave error in the results.

The substances chosen for subcutaneous injection were commercial adrenalin hydrochloride, commercial pituitary extract (obstetrical), and saline extracts of desiccated and powdered thyroid gland, pancreas and liver. The saline extracts were made by allowing 1 gm. of the desiccated powder to macerate in 100 c.c. of physiological saline solution for 24 hours at a temperature of 10° C. The mixture was centrifuged and the clear supernatant fluid was used within 24 hours. The dosage of the saline extracts was 0.5 c.c. while that of the commercial preparations was approximately 0.25 c.c.

In another paper,⁹ in which metabolic hyperglycemia was considered, it was pointed out that one of three types of reaction might follow the ingestion of considerable amounts of glucose. Since these types of reaction occur also in the hyperglycemia discussed in the present paper we shall again describe them here. In type 1 the blood-sugar values are higher at the 45-minute interval than at the zero hour, and the values at 120 minutes are as high as or higher than those at 45 minutes. With the reaction classed as type 2 the sugar concentrations are higher at 45 minutes than at the zero hour, but the values at the 120-minute interval are lower than those at the 45-minute interval. With the type 3 reaction the blood-sugar figures are lower at 45 minutes than at the zero hour and the values at 120 minutes may be lower than those at the 45-minute interval or much higher than those at the zero hour. Strictly speaking, cases occur in the type 3 group which are not hyperglycemias but hypoglycemias, the blood-sugar values never rising above the normal during the entire experiment.

In order to determine the influence of sex and age upon the various types of reaction a series of 96 rats, in which these factors were carefully recorded, was injected with adrenalin. These animals represent the adrenalin group shown in Table I. No influence attributable to these factors was demonstrable, the percentages of the various types of reaction being equally distributed irrespective as to age or sex.

⁸ Jour. Am. Med. Assn., 1914, lxiii, 1667.

⁹ Rohdenburg, Bernard and Krehbiel: AM. JOUR. MED. SC., February, 1920.

The numerical data of the experiment in which gland extracts were injected are given in Table I. This table records the actual number of animals in each group, the percentage of the various types of reaction found with each glandular extract and the average as well as the maximum and minimum amounts of blood sugar found at the different time intervals. The points of interest are (a) the wide variations between maximum and minimum in any group at any time interval, and (b) the relative constancy with which the various reaction types occur, there being practically no difference if the small number of animals used be considered.

TABLE I.

Gland extract.	No. of animals.	Percent- age of total group.	Zero hour, mg. per 100 c.c.			45 minutes mg. per 100 c.c.			120 minutes mg. per 100 c.c.		
			Av.	Max.	Min.	Av.	Max.	Min.	Av.	Max.	Min.
TYPE 1											
Adrenal . . .	32	33	135	192	90	160	206	106	190	280	108
Thyroid . . .	4	33	141	146	122	159	180	150	194	194	154
Pituitary . .	3	25	132	150	100	146	156	132	153	166	134
Liver	3	25	169	186	160	180	180	172	188	190	186
Pancreas . .	2	17	159	160	158	178	180	176	193	202	184
TYPE 2											
Adrenal . . .	31	32	136	200	84	176	262	70	116	220	100
Thyroid . . .	4	33	144	194	104	173	202	136	130	156	80
Pituitary . .	3	25	119	130	98	144	160	136	123	130	116
Liver	4	33	166	180	148	212	214	210	181	200	175
Pancreas . .	2	17	156	160	152	193	208	178	157	160	154
TYPE 3											
Adrenal . . .	33	34	155	240	102	129	194	80	141	240	86
Thyroid . . .	4	33	170	210	140	130	154	104	166	224	112
Pituitary . .	6	50	138	160	120	116	150	90	151	196	104
Liver	5	42	180	196	166	147	178	90	187	200	160
Pancreas . .	8	66	188	236	158	162	204	110	144	158	122

Hyperglycemia after adrenalin injection is not new and hyperglycemia after the injection of other gland extracts has also been described recently by French investigators.¹⁰ It is probable that the hyperglycemia after gland-extract injection is not specific but is due to the protein content of the extract, and, as we have stated before, peptone and various proteins are known to give rise to hyperglycemia. The influence of the saline used to extract the powdered gland must also be considered, and while the protocols will not be given it may be stated that in rats the injection of 0.5 c.c. of physiological saline solution does not induce a hyperglycemia. The supposed excitability of the rat, as well as the influence of from 30 to 120 seconds of ether anesthesia, which was at times used in order to enable us to hold the animals quiet, was also controlled without demonstrating a hyperglycemia caused by either condition. The experiments subsequently to be described also demonstrate that if these factors (saline injection, excitement, anesthesia) be

¹⁰ Achard, Ribot and Binet: *Compt. rend. Soc. de biol.*, 1919, lxxxii, 788.

the ones which control or induce the hyperglycemia, then we are confronted with the peculiar condition that these factors run parallel with the production of antibodies.

All that can be said of the experiments recorded in Table I is that they show that all of the substances used give rise to a hyperglycemia and that the type of reaction is not specific for any one substance.

TABLE II.

Gland removed.	Time after removal when tested.	Zero hour.	45 min.	120 min.	No. of animals.	Per cent. of type.
TYPE 1						
Adrenals complete	48 hours	126	206	212	3	43
Thyroid and part of parathyroid	34 days	139	143	151	2	33
Spleen complete	24 "	0	0	0	0	
Pancreas about three quarters	33 "	130	140	140	1	17
Thymus complete	34 "	0	0	0	0	
One kidney	34 "	150	160	160	1	9
Both testes	28 "	0	0	0	0	
Both ovaries	32 "	100	120	130	1	12
TYPE 2						
Adrenals complete	48 hours	128	223	184	4	57
Thyroid and part of parathyroid	34 days	140	164	140	4	66
Spleen complete	24 "	0	0	0	0	
Pancreas about three quarters	33 "	124	153	134	3	50
Thymus complete	34 "	140	160	130	1	20
One kidney	34 "	133	176	142	5	45
Both testes	28 "	0	0	0	0	
Both ovaries	32 "	167	171	109	5	62
TYPE 3						
Adrenals complete	48 hours	0	0	0	0	
Thyroid and part of parathyroid	34 days	0	0	0	0	
Spleen complete	24 "	172	166	152	6	100
Pancreas about three quarters	33 "	158	130	134	2	33
Thymus complete	34 "	155	139	162	4	80
One kidney	34 "	167	138	132	5	45
Both testes	28 "	158	131	156	9	100
Both ovaries	32 "	165	158	145	2	25

The second experiment consisted of repeating in part the previous determinations, this time on animals from which one or another internal secretory gland had been removed, either partially or completely. For the purpose of releasing glycogen, 0.5 c.c. of a 1 per cent. solution of peptone in distilled water was used, all other details being identical with those previously described. Table II gives the data of this group, the number of animals, the percentage of the various reaction types, the gland ablated and the average blood-sugar figures for each time period in any given group being presented.

As in the first experiment, three types of reaction were encountered, though some of the animals apparently showed some fixation of type. All of the animals in which either spleen or testes had been removed showed type 3 reaction, and 80 per cent. of the thymus-free group also came in this class. Singularly enough removal of the gonads of the female resulted in only 25 per cent. of type 3 reaction. The most violent reaction, the degree of hyperglycemia being the criterion, occurred in the adrenal-free group, the remaining animals showing less violent reactions, with the reaction in the thyroid-free group the least marked of all. In this connection it may be recalled that Janney and Isaacson have shown that removal of the thyroid inhibits hyperglycemia.

The results of the second experiment indicate that what we have chosen to call the non-metabolic hyperglycemia is not markedly influenced by removal of any of the internal secretory glands given in Table II.

In a third series of experiments, substances of widely different characteristics were injected subcutaneously into rats, in order to determine whether the list of substances causing a hyperglycemia might not be further extended. The substances used were 1 per cent. solutions in distilled water of peptone, amino-acetic acid and urea; pure olive oil, oleic acid and glycerin. The dosage was 0.5 c.c.; the last three substances, however, were used in full strength. All other details were the same as those previously described. It will be noted that all these substances, with the exception of glycerin gave rise to a hyperglycemia. (Table III.)

TABLE III.

Substance used.	No. of animals.	TYPE 1			
		Percentage of type.	Mgm. sugar per 100 c.c. blood.		
			Zero hour.	45 minutes.	120 minutes.
Peptone	0	..	0	0	0
Amino-acetic acid	1	16	106	126	162
Urea	1	16	114	140	140
Olive oil	0	..	0	0	0
Oleic acid	1	16	84	130	150
Glycerin	0	..	0	0	0
TYPE 2					
Peptone	4	40	155	203	155
Amino-acetic acid	3	50	115	151	144
Urea	0	..	0	0	0
Olive oil	2	33	152	161	135
Oleic acid	2	33	143	178	152
Glycerin	0	..	0	0	0
TYPE 3					
Peptone	6	60	194	155	180
Amino-acetic acid	2	33	143	107	150
Urea	5	84	154	125	167
Olive oil	4	66	163	141	170
Oleic acid	3	50	159	124	142
Glycerin	6	100	133	132	139

A brief study was made also of the reaction following the injection of a 1 per cent. solution of urea in distilled water in man, the Lewis-Benedict method as modified by Meyers and Bailey being used to estimate the blood sugar and the time intervals remaining as for the rats. As is shown in Table IV, variations in blood sugar followed these injections, and in one instance a variation of 33 mgm. was observed.

TABLE IV.—GLYCEMIC REACTION IN MAN AFTER INJECTION OF UREA.

Substance.	Zero hour.	45 minutes.	120 minutes.
Urea: Dose: 2 c.c. 1 per cent. solution . . .	129	112	96
	80	110	84
	92	120	102
	106	86	74
	136	129	126

Constancy of reaction type not being demonstrable with any of the substances used, our next experiment consisted of repeated injections into the same animal of different gland extracts. As is shown in Table V, even in the same individual the type of reaction is not constant when the substances injected are varied.

This last experiment was repeated on rabbits, the substance injected being a saline extract of desiccated fresh normal human liver obtained from a healthy man who had committed suicide. Blood-sugar estimations were made as before, at the same time intervals and by the same method as with the rats. The injection were given daily and in doses increasing by 0.25 c.c., the initial dose being 0.25 c.c. Three rabbits were used in the experiment; the data are given in Table VI.

Inasmuch as the matter can be much better shown by graphs, we have plotted in Chart 1 the varying reactions observed in rabbit 1 following the first five injections. It is evident that when the same substance is used for repeated injections the types of reaction encountered vary without rule. If, however, the figures for each zero hour on successive days be plotted as in Chart 2, which presents the averaged figures for the three animals, it becomes evident that with each repeated injection there is a gradually increasing hyperglycemia in which each succeeding low point is higher than the low point preceding. The 45-minute and 120-minute figures when plotted in the same manner also show this gradual increase in hyperglycemia.

Another series of three rabbits was injected with typhoid bacilli standardized at two billions per cubic centimeter. The injections were given subcutaneously every third or fourth day in increasing doses, commencing with 0.25 c.c., and increasing 0.25 c.c. every injection. Blood-sugar estimations were made as before, but at the zero hour and 60-minute interval only, and at the same time the agglutinin titer of the serum was tested. The data of the experiment

TABLE V.

Date, August.	Rat No.	Zero hour.	45 minutes.	120 minutes.	Type.
12	1	160	172	186	I
13		158	182	192	I
20		138	158	164	I
25		160	142	194	III
12	2	196	176	200	III
13		164	188	170	II
20		220	240	220	II
25		122	140	130	II
12	3	158	212	190	II
13		196	190	176	III
20		180	186	190	I
25		172	130	140	III
12	4	180	214	175	II
13		154	124	170	III
20		160	166	132	II
25		180	214	190	I
12	5	180	214	180	II
13		200	150	192	III
20		136	160	172	I
25		154	200	200	I
12	6	166	138	190	III
13		176	186	192	I
20		150	150	148	III
25		128	116	150	III
12	7	180	156	194	III
13		180	200	170	II
20		130	176	210	I
25		180	200	180	II
12	8	190	178	160	III
13		176	140	116	III
20		180	180	146	III
25		130	180	120	II
12	9	170	90	192	III
13		170	180	162	II
20		164	172	144	II
25		120	100	80	III
12	10	186	188	190	I
13		152	160	230	I
20		170	178	180	I
25		182	180	200	III
12	11	160	180	188	I
13		142	192	164	II
20		174	172	142	III
25		178	160	164	III
12	12	184	210	200	II
13		122	178	194	I
20		154	160	144	II
25		110	134	180	I

August 12, liver; August 13, pancreas; August 20, thyroid; August 25, Adrenals.

are given in Table VII and the average curves for the blood-sugar values and serum titer are shown in Chart 3. It is apparent that the progressive hyperglycemia and development of agglutinins run parallel, and that when the titer no longer increases in strength then the temporary hyperglycemia following each injection subsides, though the zero hour values may for a period remain high.

TABLE VI.—MGM. OF SUGAR PER 100 C.C. BLOOD.

Date.	Rabbit.	Zero hour.	45 minutes.	120 minutes.	Type of reaction.
2	1	112	212	230	I
4	1	124	40	136	III
6	1	210	204	190	III
8	1	136	65	230	III
10	1	194	196	280	I
12	1	236	250	220	II
15	1	150	150	152	III
17	1				
18	1				
19	1	210	...	190	
25	1	220	...	190	
2	2	116	340	194	II
4	2	116	48	124	III
6	2	...	220	216	
8	2	186	242	104	II
10	2	140	158	208	I
12	2	264	
15	2	220	226	240	I
17	2	240	...	260	
18	2				
19	2				
25	2	110			
2	3	65	230	234	I
4	3	156	48	112	III
6	3	220	200	200	III
8	3	170	136	156	III
10	3	170	198	214	I
12	3	152	...	136	
15	3	238	280	240	II
17	3				
18	3				
19	3	210	...	188	
25	3	115			

Another series of three rabbits was injected with 2 c.c. of a 5 per cent. suspension of sheep red blood cells, injections being made subcutaneously in uniform dosage. At stated intervals blood-sugar determinations and lytic titers were done, the time periods being the same as with the rabbits injected with typhoid vaccine. The data of the experiment are given in Table VIII and graphically shown in Chart 4. Again, it is evident that the increasing hyperglycemia follows the development of lytic substances.

CONCLUSIONS. From the experiments recorded it may be concluded that a temporary hyperglycemia accompanies the injection

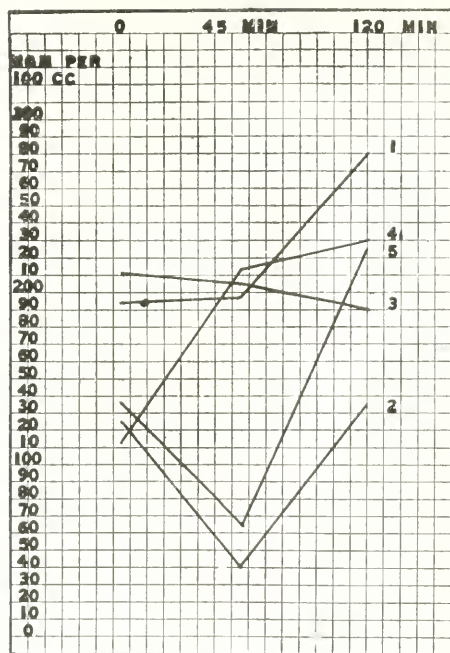


CHART 1
 SHOWING DIFFERENT TYPES OF
 REACTION FOLLOWING SUCCESSIVE
 INJECTIONS OF THE SAME SUBSTANCE

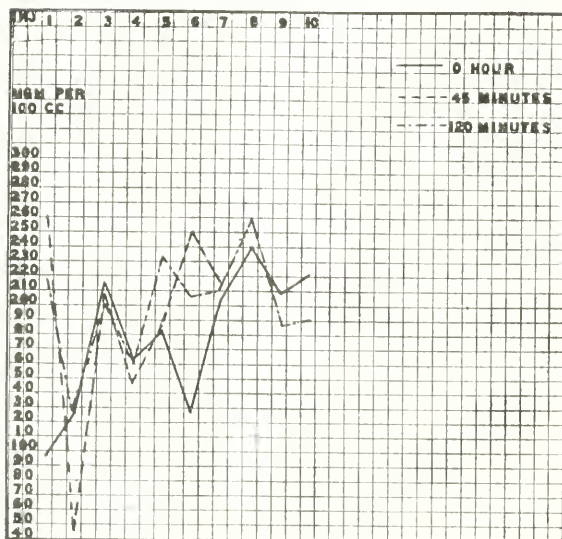
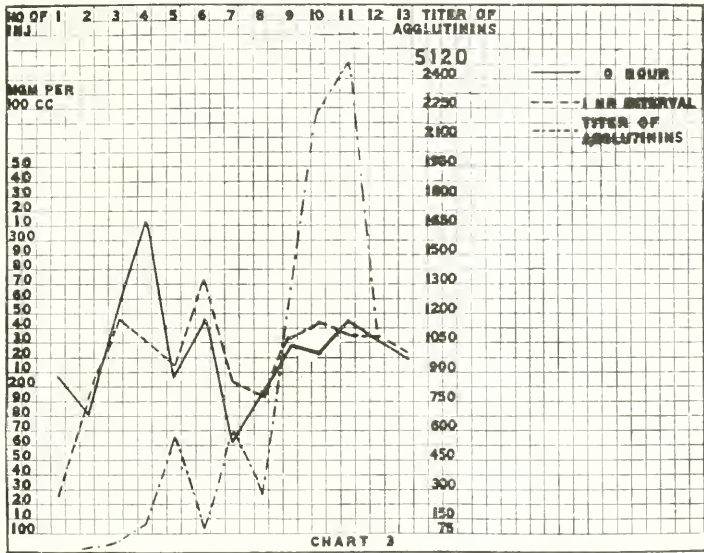


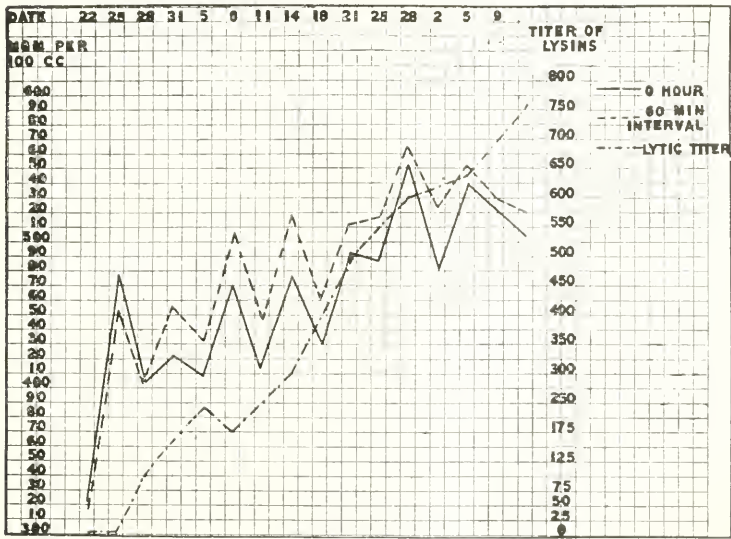
CHART 2

of a variety of organic and inorganic substances. The reaction type encountered is not specific for any given substance injected,

COMPARISON OF BLOOD SUGAR CURVES AND AGGLUTININ TITER



BLOOD SUGAR CURVE AND CURVE OF LYCIC TITER



nor can a reaction type be said to be distinctive of lack of function of any one of the endocrine glands tested. Repeated injections of

the same substance cause a gradual rise in the blood sugar parallel to the formation of agglutinins or lysins. Irregular fluctuations occur in the sugar content of the blood from day to day, but, as shown in Chart 4, the trend is upward until the maximum titer of antibody is reached, no glycemic reaction following the further injection of the substance used. Whether this hyperglycemia is due to temperature variations which are known to follow the ingestion¹¹ or the injection of foreign protein,¹² or whether it is due to the breaking up of protein which occurs in the process of antibody formation, cannot at present be definitely stated.

TABLE VII.—MGM. OF SUGAR PER 100 C.C. OF BLOOD.

Date.	Rabbit.	Zero hour.	60 minutes.	Agglutinin titer.
22	1	210	130	
24	1	196	170	
27	1	188	202	80
1	1	266	260	160
5	1	210	230	320
8	1	240	280	80
11	1	120	160	1280
15	1	258	224	640
18	1	210	230	1280
23	1	220	230	5120
28	1	234	234	5120
1	1	220	230	1280
4	1	228	230	
22	2	248	144	
24	2	202	194	
27	2	226	222	20
1	2	224	236	40
5	2	200	180	1280
8	2	280	300	80
11	2	160	250	320
15	2	210	216	60
18	2	236	240	320
23	2	200	230	280
28	2	256	248	5120
1	2	244	250	640
4	2	240	244	
22	3	166	108	
24	3	146	200	
27	3	216	250	80
1	3	228	200	160
5	3	213	230	80
8	3	220	240	160
11	3	200	210	
15	3	140	144	160
18	3	240	226	80
23	3	250	270	1280
28	3	246	250	1280
1	3	228	224	5120
4	3	204	200	1280

¹¹ Atkinson and Lusk: Jour. Biol. Chem., 1918, xxxvi, 415.

¹² Zinsser: Infection and Resistance, New York, 1918.

The experiments here recorded show a phenomenon associated with the process of immunity which has hitherto escaped observation. An analysis of the hyperglycemia following repeated injections of the same substance indicates that the hyperglycemia is one which gradually increases in intensity up to a certain level of sugar concentration in the blood, that it keeps this level of intensity

TABLE VIII.—MGM. OF SUGAR PER 100 C.C. OF BLOOD.

Date.	Rabbit.	Zero hour.	60 minutes.	Lytic titer.
22	1	380	316	
25	1	480	480	
28	1	428	440	100
31	1	436	456	200
5	1	408	460	200
8	1	496	520	200
11	1	460	476	
14	1	480	520	400
18	1	456	468	
21	1	480	496	600
25	1	480	500	
28	1	560	588	900
2	1	520	540	
5	1	544	560	1200
9	1	536	556	
12	1	528	528	1400
22	2	336	300	
25	2	516	460	
28	2	388	376	100
31	2	420	440	100
5	2	396	400	200
8	2	480	520	200
11	2	366	420	
14	2	472	520	200
18	2	396	416	
21	2	520	540	300
25	2	508	540	
28	2	544	552	400
2	2	480	596	
5	2	516	536	300
9	2	500	500	
12	2	500	508	400
22	3	248	340	
25	3	456	420	
28	3	396	396	100
31	3	412	472	200
5	3	420	440	300
8	3	464	484	200
18	3	440	500	
21	3	480	500	600
25	3	476	516	
28	3	552	560	500
2	3	440	440	
5	3	560	560	400
9	3	536	536	
12	3	496	496	500

The blood-sugar values are considerably higher in this group because 0.05 c.c. of blood were used instead of 0.2 c.c. as with the others. The smaller the amount of blood used the higher the normal values, has been our experience.

for a short period and then returns to a normal figure even though the immune bodies are still present in the blood. The experiments further suggest that the hyperglycemia which follows the injection of substances generally supposed not to be capable of inducing antibody formation (*i. e.*, fats, polypeptides) may serve as a method for testing the reactions of the body when neither precipitins, agglutinins nor lysins are demonstrable. From a practical standpoint the absence of a hyperglycemia after the injection of a given substance known to induce hyperglycemia might be taken to indicate the point of maximum antibody production in the individual or animal in question.

OBSERVATIONS ON SOME TESTS OF PHYSICAL FITNESS.

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CERTAIN facts of considerable interest were obtained from tests carried out in France at U. S. Base Hospital No 6 during the summer of 1918.¹ At first plans for careful work were hopefully made, but the routine became soon so overwhelming that only the initial tests could be completed satisfactorily. Because of two or three important conclusions to be drawn from these tests and from the observations that followed I am making this report.

In June and July, 1918, I took over the care of the gassed cases, chiefly those convalescent, and continued this work until after the Armistice. The first task was to organize the wards, which shortly developed into a camp of several hundred patients. By October I was swamped by 500 cases in the clinic at one time, but the routine was developed satisfactorily.

The second task and the more important was to decide at what time the soldiers were fit to return to combat duty; or when they should be reviewed by the Disability Board for assignment to special duty under the classification B-1, B-2; C-1, C-2; or for return to the U. S. A. as of Class D.

A signified fitness for combat or active normal duty.

B-1 signified temporary non-combat normal duty.

B-2 signified temporary non-combat light duty.

C-1 signified permanent non-combat normal duty.

C-2 signified permanent non-combat light duty.

As time went on during the summer, work on the "gassed" cases became organized and convalescent patients from the other hospital wards were then sent to me to benefit by the exercises, games and

¹ I wish to express my appreciation for the great assistance rendered to me by Sergeant John O. Moose.

semi-military life. Eventually, my patients included "gassed" cases, convalescents from infectious diseases, patients with healing chest wounds, effort syndrome cases and a few other neurotics. About three-quarters of the cases were discharged to Class A duty and the rest were about evenly distributed, as Class B-2, Class C-2, and Class D by the Disability Board. The work proved to be successful. Some following up of the cases was begun, but was interrupted by the Armistice. Cards were printed and given to the soldiers discharged from these convalescent and "gassed" wards to be sent back after two weeks of duty. The replies indicated generally that the method of classification was satisfactory.

Tests. I shall now describe in detail the tests which we tried out before we decided finally on the ones that were the most practical. First we made a number of tests on several groups of young soldiers of average age, height and weight. One group consisted of five normal men; one of five convalescent "gassed" soldiers; one of five effort syndrome cases; and one of five psychoneurotic "shell-shock" soldiers. The tests were those of exercise and respiration, the latter following tests the British Aviation Service was using.

The respiratory tests were:

1. Breath-holding: length of time in seconds that the breath could be held.

2. Vital capacity: the amount in cubic centimeters of air that could be expelled from the chest after a maximum inspiration.

3. Expiratory force: as determined by the height in milligrams to which a mercury column, 4 mm. in diameter, could be blown.

4. Fatigue test: the length of time in seconds that the mercury column could be held by the respiration at 20 mm. height.

5. The amount of fluid (liquid paraffin) in cubic centimeters that could be blown over from one bottle into another. This combined the fatigue test factor and the vital capacity factor. This test was not one of the British Aviation Service.

The exercise tests as planned included:

1. Climbing two flights of steps in one minute of time, fifty steps in all, each one 16 em. high.

The pulse-rate, respiratory-rate, systolic and diastolic blood-pressure and subjective sensations were noted before the exercise, immediately at the end of the exercise and two minutes and five minutes after the end of the exercise.

2. 100-meter walk and 100-meter run (dog trot) with the gas mask on.

The pulse-rate and general condition were recorded.

3. 5-kilometer march.

The pulse-rate, blood-pressure and general condition noted before and after.

We had hoped to carry out the 5-kilometer march test with the pack on, but the routine of work prevented.

TABLE I.—SUMMARY OF RESPIRATORY AND EXERCISE TESTS IN FOUR GROUPS OF SOLDIERS: NORMAL; CONVALESCENT "GASSED"; "EFFORT SYNDROME," AND PSYCHONEUROSIS WITH "SHELL SHOCK." AVERAGE FIGURES.

Group.	Respiratory tests. ²				Exercise tests.																			
	Holding breath, time in seconds.	Vital capacity in c.c.	Mercury column; expiratory force; height in mm. to which mercury column can be blown.	Mercury column; fatigue test; time in seconds, during which column kept at 20 mm.	Blow-bottle test: c.c. of paraffin oil blown from one bottle into another.	Pulse-rate.			Respiratory-rate.			Blood-pressure.		Gas mask on.		5-kilometer march, 1 hour.								
						Increase (pulse-rates).	Decrease after 2 minutes' rest.	Increase (respiratory rates).	Decrease after 2 minutes' rest.	Increase in mm. Hg. (systolic pressure).	Decrease after 2 minutes' rest.	Change at once (diastolic pressure).	Change after 2 minutes' rest.	At rest.	After 100-meter walk.	After 100-meter run (dog trot).	Before.	After.	Before.	After.				
Normal, 5	73	4750	157	63	154	19	21	2	2	11	13	-8	+1	81	92	128	71	97	127	125	85	86		
British Aviation figures (normal)	66	4000	110	52																				
				at 40 mm.																				
Effort syndrome, 5	41	3250	64	21	81	28	30	9	6	17	10	-5	+6	87	115	144								
Convalescents from gassing, 5	32	2840	71	14	80	17	18	5	4	13	13	+2	0	76	101	128	72	88	105	107	68	77		
Neurotics ("shell shock"), 5	13	2240	23	6	31	19	17	17	5	18	17	+1	3+	Because of nervousness could not keep masks on										

² The figures are the averages of three trials in each respiratory test. This applies also to the four other tables.

TABLE III.—DETAILED TESTS IN FIVE SOLDIERS WITH MILD "EFFORT SYNDROME."

Group.	Respiratory tests.					Exercise tests.															
	Holding breath, time in seconds.	Vital capacity in c.c.	Mercury column; expiratory force; height in mm. to which mercury column can be blown.	Mercury column; fatigue test; time in seconds during which column kept at 20 mm.	Blow-bottle test: c.c. of paraffin oil blown from one bottle into another.	Pulse-rate.		Respiratory-rate.		Blood-pressure.				Gas mask on.		5-kilometer march, 1 hour.					
						Increase (pulse-rates).	Decrease after 2 minutes rest.	Increase (respiratory rates).	Decrease after 2 minutes rest.	Increase in mm. Hg. (systolic pressure).	Decrease after 2 minutes rest.	Change at once (diastolic pressure).	Change after 2 minutes rest.	At rest.	After 100-meter walk.	After 100-meter run (dog trot).	Before.	After.	Before.	After.	
All soldiers.						Increase (pulse-rates).	Decrease after 2 minutes rest.	Increase (respiratory rates).	Decrease after 2 minutes rest.	Increase in mm. Hg. (systolic pressure).	Decrease after 2 minutes rest.	Change at once (diastolic pressure).	Change after 2 minutes rest.	At rest.	After 100-meter walk.	After 100-meter run (dog trot).	Before.	After.	Before.	After.	
	N.	48	3400	65	17	37	14	16	18	16	20	5	-12	116	122	184					
	R.	70	4700	70	43	57	20	32	4	0	16	14	-9	72	100	120					
	I.	35	3450	130	10	60	44	32	8	2	34	14	0	8	60	120	130				
	McK	42	3350	100	35	160	24	28	10	10	14	16	-4	6	78	112	156				
R.	10	1350	40	0	8	40	40	3	2	2	0	0	0	108	120	129					
						80-120-80		15-18-16			136-138-138		72-72-72								

Average weight and height.

TABLE IV.—DETAILED TESTS IN FIVE SOLDIERS CONVALESCENT FROM "GASSING."

Group.	Respiratory tests.				Exercise tests.																
	Holding breath, time in seconds.	Vital capacity in c.c.	Mercury column; expiratory force; height in mm. to which mercury column can be blown.	Mercury column; fatigue test; time in seconds during which column kept at 20 mm.	Flow-bottle test; c.c. of paraffin oil blown from one bottle into another.	Pulse-rate.		Respiratory-rate.		Blood-pressure.		Gas mask on.		5-kilometer march, 1 hour.							
All soldiers.	7	2000	50	4	20	Increase (pulse-rates).	Decrease after 2 minutes rest.	Increase (respiratory rates).	Decrease after 2 minutes rest.	Increase in mm. Hg. (systolic pressure).	Decrease after 2 minutes rest.	Change at once (diastolic pressure).	Change after 2 minutes rest.	At rest.	After 100-meter walk.	After 100-meter run (dog trot).	Pulse-rate.	Blood-pressure in mm. Hg.			
																		Systolic.	Diastolic.	Before.	After.
V. Mustard gas 2 weeks ago; dyspnea, weakness and dizziness; burn of neck; no cough; lungs clear						12 80-9.8-86	6 30-4-2-36	6 30-4-2-36	6 30-4-2-36	10 104-11-4-100	14 104-11-4-100	-6 74-6.8-58	-10 74-6.8-58	72	130 Faint	Not tried	76 112 100-102 Fall out for rest	72 78	72 78	Before. After.	Before. After.
W. N. Mustard gas 10 days ago; dyspnea, skin burns, conjunctivitis; lungs clear	19	2500	50	18	50	14 88-10.2-76	10 22-3-2-26	10 22-3-2-26	6 22-3-2-26	10 96-10.6-104	2 96-10.6-104	+8 60-6.8-84	+16 60-6.8-84	84	112	148	66 84 100-102 Fall out for rest	68	68	Before. After.	Before. After.
T. M. B. Mustard gas 2 weeks ago; cough, hoarseness, burns of scalp; heart and lungs clear	23	2500	50	10	65	30 90-12.0-38	3 21-2-1-19	5 21-2-1-19	5 21-2-1-19	18 112-13.0-104	26 112-13.0-104	0 80-8.0-80	0 80-8.0-80	84	90	130	81 90 116 125 80 98	98	98	Before. After.	Before. After.
C. C. Phosgene gas 10 days ago; dyspnea and slight cough; heart and lungs clear	83	4000	200	25	180	18 58-7.6-54	0 20-2-0-19	1 20-2-0-19	1 20-2-0-19	9 103-11.2-105	7 103-11.2-105	-2 60-5.8-60	+2 60-5.8-60	56	72	104	52 63 104 104 60 Exercised to exhaustion	70	70	Before. After.	Before. After.
J. E. H. Mustard and phosgene gases 2 wks. ago; cough, hoarseness, neck burns; heart and lungs clear	29	3100	50	11	40	10 84-9.4-80	5 19-2-1-19	5 19-2-1-19	5 19-2-1-19	20 90-11.0-94	16 90-11.0-94	+10 50-6.0-52	-8 50-6.0-52	82	100	130	84 92 107 102 62 Good condition	70	70	Before. After.	Before. After.

Discussion of Results. From the tables it is obvious that the cases most strikingly limited in capacity in nearly all of the tests were the "shell-shock" cases of psychoneurotics. Incidentally the convalescents from acute infectious disease, as a rule, did well in the exercises or games tried and went back to duty more quickly than any of the others, provided there was no pronounced neurotic element as an additional factor. It always proved of extreme importance to look for nervousness in all cases convalescent from any condition. Such nervous cases, although apparently recovered, generally responded poorly to the tests, and really were not fit. Such people were often bright, capable of careful mental work, but not for the strenuous physical war game. Race seemed often a factor.

All these tests appeared to be much more tests of the fitness of the nervous system than of the heart and lungs *per se*. To stimulate convalescence and to obtain an excellent test for malingering (which was usually of the unconscious type and not infrequently found), base-ball games were held about twice a week, the wards playing against each other, and as many substitutes used in the game as possible. The medical officer kept score on the side lines, thus closely following individual players. Some of the games were exceedingly close and interesting, and usually the men in the midst of the play forgot their symptoms. Some of them showed themselves easily fitted who had been complaining previously a good deal, while others were obviously exhausted by dash to the first or second base, for example. Games such as these, followed closely, prove an excellent stimulus as well as a test for physical fitness.

The test which we finally employed as the best, taking into consideration exertion, excitement and the need of economy of time and effort on the part of the medical officer, was the 100-meter run with the gas mask on. The run provided the exertion and the gas mask the mental spur. Bad general appearance, breathlessness, pain, faintness, cough, extreme tachycardia and exhaustion were the conditions looked for at the finish of the run and helped decide on the fitness of the individual. This test was used on about 2000 soldiers.

There is one further observation that I should like to make. Many of the soldiers, I should hazard probably one-third, sent down to our Base Hospital as gassed, showed only nervousness when they reached the hospital. It is quite likely that that was all that was troubling many of the A. E. F. who said that they had been "gassed."

Summary. 1. Various tests, respiratory and exercise, are described which were applied in U. S. Base Hospital No. 6, A. E. F., to small groups of normal soldiers, convalescent "gassed" soldiers and to neurotics of the "effort syndrome" and "shell-shock" types.

2. The 100-meter run with the gas mask on was the test finally chosen as the most practical for use at U. S. Base Hospital No. 6 in determining the fitness of the soldier to return to combat duty.

3. All the tests proved to be tests rather of stability of the nervous system than of cardiac and pulmonary condition *per se*: the more nervous a man the poorer his reaction.

4. One of the most important applications to civilian medicine of the lessons from these tests is with respect to the vital capacity, which proved to be rather a test, as mentioned above, of nervous stability than of the condition of the cardiovascular or respiratory systems *per se*, in the groups under discussion.

LIFE-CYCLES OF THE BACTERIA AND THEIR POSSIBLE RELATION TO PATHOLOGY.

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VERY early in the history of bacteriology the belief prevailed that the various morphological units were quite interchangeable, *e. g.*, rod forms easily developed into coccus forms, and *vice versa*. As bacteriological methods were improved it became evident that in the majority of instances these changes were apparent only—that when a bacterial species or type was once isolated and subsequent contamination guarded against the induction in it of cultural and biological changes was no simple matter. In other words a pure culture, under the artificial conditions of the laboratory, would “breed true” to the characteristics that had fixed its specific ranking.

As a result the theory of fixity or immutability of bacterial types has gradually supplanted the primitive view of an unrestrained plasticity of bacterial protoplasm. For the designation of the curious but fluctuating changes in form displayed by pure cultures when subjected to variations of environment we have the term polymorphism or pleomorphism, while the term involution is applied to the bizarre forms often present in old cultures. The latter were regarded as degenerated forms, usually incapable of reproduction, and as such the counterpart of a deterioration in the nutritive qualities of the medium.

For several decades these fundamental ideas have completely dominated our conceptions of bacteria in relation to disease. The simple processes of transverse fission and spore formation have been thought to embrace practically the entire truth concerning the life-history of bacteria. Despite these facts, there has always existed a residuum of workers, who, unable to doubt experimental evidence, have not yet been entirely convinced that the story was so simple—
ho have felt that, bound up in some way with these curious morphological changes, were fundamental biological principles, which

when formulated might clarify many of the problems of infection that have been clouded so effectually by the terms pleomorphism and involution.

Scattered through the literature can be found instances, not infrequent, of observers who have found it necessary to invoke some sort of cyclic or phasic change, physiological in nature, to explain satisfactorily the conditions confronting them. But it is only within relatively recent years that any systematic efforts have been directed toward the solution of these problems, and the number of workers is but few indeed. It is not the intention of this paper to consider in any exhaustive way the literature of the subject but merely to attempt a preliminary integration of the more significant studies already made, with allusions to their possible bearing on some of the unsolved problems of present-day pathology and bacteriology.

The studies to which I wish to direct attention date back to 1914-15 or thereabouts and have been conducted chiefly by Hort, Löhmis and their co-workers and the writer. Hort's work¹ deals chiefly with the meningococci, the colon-typhoid-dysentery group and with typhus fever. He believes that the meningococcus, as we know it, is not the primary cause of epidemic cerebrospinal fever, because he is unable to produce the disease in monkeys by intraperitoneal injections of laboratory cultures of the organism, or, for that matter, in any other way. Flexner's intraspinal inoculations produced meningitis only, which is but one part of the disease. But even these results he considers at best inadequate and probably fallacious, on account of the enormous quantities of organisms used, lysis of which caused a toxic meningitis only. Flexner refers to the doses used as "colossal," also expressing himself as "disinclined to believe that in many of the experiments any multiplication whatever took place." Hort, furthermore, discounts the value of such meningeal inoculation in light of the ease with which meningitis is induced in monkeys by other organisms.²

On the other hand he shows that the cerebrospinal fluid of patients contains a filtrable virus which, in the fresh state, will initiate a continuous fever in monkeys when it does not actually cause death; but inoculation of this filtrate will then yield the meningococcus, in addition to other forms encountered in this disease, such as the well-known diplococcus of Jaeger. These results suggest to him that the virus and the meningococcus are phases in the life-cycle of one organism.

¹ Hort and Ingram: The Etiology of Typhus Fever, *British Med. Jour.*, May, 1914. Hort: Typhus Fever, *British Med. Jour.*, 1915. Hort, Lakin and Benians: Epidemic Cerebrospinal Fever: The Place of the Meningococcus in its Etiology, *British Med. Jour.*, March 27, 1915 and April 24, 1915. Hort: The Relation of the Meningococcus of Weichselbaum to the True Infective Agent in Epidemic Cerebrospinal Fever, *Jour. Roy. Med. Corps*, February, 1916. Hort: The Life History of Bacteria, *British Med. Jour.*, May 5, 1917.

² The citations and opinions here expressed of Flexner's works are Hort's.

He believes this organism, which he places among the ascomycetes, has a mycelial or bacillary stage; but adequate study of this phase has not yet been made. In this connection it is pertinent that the very large "coccoïd" forms described in the spinal fluid have always been regarded as involutionary, but, as the result of warm stage studies on them, Hort believes that they are giant or spurious meningococci and that they give rise by endosporeulation to the true meningococci, being inseparable concomitants of the latter. He also regards this giant form as the antecedent of a filtrable form. He is not certain that the latter develops directly into true meningococci, but it "appears, however, to form a connecting link between invisible filtrable virus and Weichselbaum's organism."

From my own viewpoint it would seem that, in order to demonstrate this contention with finality, it would almost be necessary to grow this ascomycete apart from the meningococci and to show that it is possible for it to pass through the evolutionary cycle which terminates in true meningococci and the virus. He has also shown that certain members of the colon-typhoid-dysentery group reproduce themselves in other ways than by simple binary fission and that the life-cycle includes in some cases an invisible phase. By employing an especially acid medium he brings about aberrant morphological types which he considers physiological variants, particularly since these types maintain their "aberrancy" for several generations when transferred to their original environment.

He has rejected in his work the employment of the Barber method for the isolation of single bacterial cells, owing to its inadequacy in the presence of invisible or very minute forms. Although this contention may be justified in cultures associated with perfectly demonstrable filtrable forms, I feel that the cultures should be started from single cells of the strain in its non-filtrable stage, if it has such a stage. At any rate, I have adopted this criterion in my own studies, if for no other reason than to forestall criticism, undoubtedly legitimate, especially in the present unsatisfactory state of knowledge of the filtrable forms and their relation to the larger forms.

Löhuis³ in a preliminary study attacks the subject entirely from the morphological side, with the exception of some filtration experiments not yet complete. He states that all bacteria studied have been found to alternate in an organized and in an amorphous stage, from which stage in all cases "regenerative units" develop, and increasing in size turn into "regenerative bodies" which later become cells of normal shape. Direct union of two or more individual cells has also been observed. All bacteria are found to multiply, not only by fission, but also by the formation of "gonidia," which

³ Life Cycles of the Bacteria (Preliminary Communication), Jour. Agricultural Research, July 31, 1916.

usually first become regenerative bodies, but sometimes grow directly to full-sized cells. The gonidia may be liberated either by complete or partial dissolution of the cell wall, or may develop while still united with their mother cell. A more analytical review of his work will not be entered into here, inasmuch as his study concerns itself with *B. azotobacter*, which, of course, is non-pathogenic. The biological principles involved, however, are the same, and for this reason his work is of suggestive import. Confirmations of a physiological nature he promises for subsequent papers.

The work of Ferran⁴ and of Much⁵ on the tubercle bacillus is also deserving of mention in this connection. The work of the former extends over the past two decades, and he has concluded that this organism includes in its life-history three distinct stages: First, the alpha bacillus, which is non-acid-fast and which he believes has very distinct immunizing properties in the early stages of the disease. The second stage is represented by the well-known non-acid-fast but Gram-positive granules of Much, and the third stage is the tubercle bacillus as ordinarily considered. In connection with the supervirulence attributed by Much to his granules, it is of value to recall again what has become a very common experience: that acid-fast bacilli often utterly fail of demonstration in material that on inoculation produces a virulent form of tuberculosis. Furthermore, heating the material to 80° C. renders it innocuous, proving that the result cannot be accounted for on the spore basis.

The writer's work has been an outgrowth of studies with the so-called *B. hodgkini* and related diphtheroid strains, although fusiform bacilli and streptothrices have also occupied my attention. I am attempting to attack the problem not only from the morphological and cultural sides, but from the immunological and pathological aspects as well.

My first study dealing with the phenomena in question appeared in 1917,⁶ being a consideration of remarkable morphological and biological changes in a diphtheroid organism whereby the bacillary form was transformed into a diplococcus form, having somewhat different characteristics from the bacillus. One of the earliest changes observed in the bacillus was a gradual concentration of the chromatin granules, which in some cases went so far as to form a single large giant coccus. Long filamentous forms suggestive of the higher organisms were sometimes observed. The press of other features of this study precluded a more detailed investigation of the significance of these coccoids, which often assumed a size of

⁴ Travaux sur la Nouvelle Bacteriologie de la Tuberculose, Barcelone Imp, "La Rensixensa," 1913, 13.

⁵ Beit. z. Klinik d. Tuberculose, 1907, viii, 85-357, 368; 1908, xi, 67; 1913, supplement, vol. vi.

⁶ A Study of the Diphtheroid Group of Organisms, etc., Jour. Bacteriol., 1917, Nos. 2, 3 and 4, vol. ii.

5 or 7 μ . The diplococcus phase of this organism reproduced itself as such and the whole phenomenon strongly suggested a mutation; but from the fact that under certain conditions the bacillary form again appeared, I did not then feel justified in regarding it as such. I should add that, when in the diplococcus form, this organism not only appeared as a streptococcus but was related pathogenically and immunologically to a certain non-hemolytic type, and I concluded that a biological linking exists between these two groups.

During the experiments I occasionally observed that the organism was filtrable. This feature of the work also had to be put aside for later study. All these rather unusual phenomena suggested to me at the time that some phasic or cyclic change might later become a necessary explanation, though I preferred to go no further in interpretation than an extreme pleomorphism. My subsequent studies with this and related organisms have convinced me that such an explanation is quite inadequate for the scope of the changes involved.

In an experimental study of a case of generalized streptothricosis⁷ I have shown that a filtrable form was present in the blood, which, however, when cultivated grew as a diplococcus, the latter being experimentally changed to the filamentous or branching form. A granular or diphtheroid form was also isolated which could be changed into large coccoids, and from these the filamentous form again developed. I have regarded these separate entities with distinctive characteristics as stages in the life history of a single organism. Preliminary to these transformations the organism usually went into the giant coccus phase, which has been frequently observed among diphtheroid bacilli. I have brought forward presumptive evidence to show that these coccoids are not involution or pleomorphic, as ordinarily considered. Warm stage observations correlated with protozoal stains have developed evidence that they are capable of a very complex series of changes connected with reproduction of various stages of the organism not the least important of which being the filtrable phase found in the blood stream.

Another separate order of filtrable body or gonidium was described for the diphtheroid stage. These gonidia originated apparently between the chromatin granules. I have regarded them as comparable with Much's granules of the tubercle bacillus. Although their pathogenicity will be described in a future paper, I may anticipate to the extent of saying that they were definitely virulent under conditions that showed the bacillary phase to be quite innocuous.

The branching phase also gave rise to filtrable granules by budding, which was of special interest in that they could not be culti-

⁷ Mellon, R. R.: Contribution to Bacteriology of a Fusospirillary Organism, with Special Reference to its Life History, *Jour. Bacteriol.*, 1919, iv, 505-536.

vated beyond the first generation. This, to my knowledge, is the first evidence that trichomyces infections may have a filtrable phase; and it may explain our inability in the past to infect experimental animals with members of this group. In a paper entitled "The Prevalence of Trichomyces Infections in Western New York,"⁸ several other cases were studied with this same idea in mind. Although the more detailed experimental studies on some of them will be given at a later time the evidence presented was in harmony with that given for the fusospirillary organism (streptothricosis).

Heinemann⁹ working with *B. diphtheria*, was able to confirm my findings in part. He noticed that his culture was losing in toxicity, which seemed to be correlated in some way with the fact that it had assumed temporarily a coccus morphology. W. W. Browne¹⁰ has recently described a chromogenic spirillum that lived and reproduced itself as a coccoid under altered conditions. It is of interest that it was no longer pigment-producing while in this stage and was physiologically different in other ways. It is but fair to state that Ebersson¹¹ was not able to confirm my findings with the diplococcus transformations and vigorously refutes my work, chiefly on the ground that I had not used the single-celled isolation method for purifying my cultures. It is not the province of this paper to go further into his work and its relation to my own; suffice it to say that in forthcoming communications I shall show by the use of the single-celled method that the facts as I presented them were essentially correct, and will demonstrate also, more completely than has yet been shown, the mechanism of these changes with their relation to bacterial life-cycles and to mutation and variation among the bacteria.

RELATION OF THESE STUDIES TO THE PROBLEMS OF PATHOLOGY. From the strictly utilitarian standpoint the origin of the various races of bacteria may be of little moment. As one man expressed it "We know that the diphtheria bacillus as such produces a toxin that can be neutralized, and whether or not it is a stage in the life-cycle of something else is of scant interest to human pathology." As those of us who are most interested in such subjects develop them further, I trust that such a viewpoint will have progressively fewer supporters than at present. This tendency of the purely medical bacteriologist to interest himself solely in pathogenic organisms has been particularly unfortunate in many ways, not the least being an indifference to some of the broader concepts of biology, little realizing that their application might bring him much

⁸ Mellon, R. R.: The Prevalence of Trichomyces Infections in Western New York, *AM. JOUR. MED. SC.*, April, 1919, No. 4, clvii, 540.

⁹ *Jour. Bacteriol.*, No. 4, ii, 361-363.

¹⁰ Program of Annual Meeting of Society of American Bacteriologists, Boston, 1919.

¹¹ *Jour. Infect. Dis.*, 1918, xxiii, 1-42.

nearer to the solution of problems in infection that have long constituted an insuperable obstacle to the advance of "practical bacteriology."

Let us consider for a moment the relatively unexplored realm of the viruses, so called, particularly with reference to certain "accompanying saprophytes" or "secondary invaders." We know that in hog cholera the *B. suispestifer* is constantly present in the intestines of these animals, and their blood serum shows immune reactions to these organisms. We also know that they are present in the intestines of other healthy animals at such periods of infection which might be considered as carriers. Yet it has been conclusively shown that a filtrable virus is the exciting cause of hog cholera, with the *suispestifer* having no relation to the disease except as a secondary invader. An epizootic of infectious abortion in guinea-pigs with an organism resembling *suispestifer* constantly present was proved by Petri and O'Brien¹² to have been caused by a filtrable organism.

It is well known that a streptococcus is a constant concomitant of scarlet fever and that immune reactions can be demonstrated in the blood of many of these cases, and streptococcic vaccines have been declared by some to have prophylactic value. Yet the streptococcus is not regarded as the primary causative agent. Likewise it has been well established that a diphtheroid organism is consistently to be isolated from the glands and blood in cases of Hodgkin's disease and certain other affections of the blood organs. Yet to date, Hodgkin's disease has not been successfully reproduced. In typhus fever practically the same set of conditions exists. The fresh-blood filtrates seem to have reproduced the disease in monkeys (Hort), whereas the incubated filtrates in which *B. exanthematicis* appears have relatively little effect on this animal. (Hort.)

Just what is the significance of the presence of certain specific types of organisms associated with certain diseases, in most of which they are not considered as the primary causative agent? According to the present current views of "fixity of bacterial types" they have been considered, and logically so, as purely complicating factors in the diseases in which they occur. But if we take the view, evidence for which is slowly but certainly increasing, that bacteria have other means of reproduction than simple fission, we predicate at once that their life-history can be a matter of developmental phases, in which case we are free to assume, at least, that the virus, *e. g.*, of hog cholera, may be a filtrable phase in the life-history of *B. suispestifer*, etc.

It would modify profoundly our conception of the causation of a disease like influenza and might open the way toward establishing the actual relation of *B. influenza* to the disease. Indeed, a suggestion of this sort has recently appeared in the work of Wade and

¹² Jour. Hyg., 1910, vol. x.

Manalang,¹³ who have shown that certain strains of this organism can by alteration of their environment be made to branch and assume other characters usually allocated to the higher bacteria.

Such a conception would be of value in the interpretation of the peculiar symptom-complexes presented by certain conditions of obscure etiology. The striking remissions of pernicious anemia, the Pel-Ebstein febrile complex in Hodgkin's disease as well as the spontaneous and clinically deceptive retrograde changes observed in this and related diseases, might well be correlated with alternate "resting stages" and stages of activity in the life-history of organisms whose adaptability was thus mirrored.

The relapsing type of fever associated with certain spirochete infections, *e. g.*, *Sp. obermeiri*, might thus find explanation, although this citation may be infelicitous, owing to certain taxonomical uncertainties of these forms. It may be recalled in this connection that Noguchi found "coccoïd" bodies in his cultures of *pallida* and, that Warthin¹⁴ has found what might be regarded as such in tissues devoid of the typical *pallida* but almost undoubtedly syphilitic.

The regular periodic febrile exacerbation characterizing the streptothrix infection of rat-bite fever, and the irregularly intermittent fever of other thrix infections, following deceptive clinical cures; the strong tendency to recurrence in fusiform infections may be explained on a similar basis; for these phases of activity, if such they be, must have immunological counterparts in the host.

It is not improbable that "bacterial fastness" to therapeutic agents, and to the immunological forces of the body, can perhaps be correlated with these changes in phase. It is well known, for example, that the spirochetes that survive salvarsan treatments acquire an increased resistance. The granules of Much may be a "reply" of the tubercle bacillus to the lipases of the lymphocytes. In an unpublished study I have shown that the bacillary phase of a certain diphtheroid was Gram-positive, but the diplococcus phase was Gram-negative. These cultures were started from single cells and the strains were made of twelve-hour cultures. Thus, immunologically, phases and stages of bacterial life may have a distinct bearing on the course of a disease.

The rather constant presence of a non-acid-fast diphtheroid organism in leprosy is not susceptible at present of final interpretation. Bayon (Besson)¹⁵ and Williams (Besson)¹⁶ regard them as a probable stage in the life-cycle of the Hansen bacillus, while Kedrowski¹⁷ believes he has proved that they take on acid-fast characters in the

¹³ Jour. Exper. Med., No. 1, xxxi, 95-103.

¹⁴ Personal communication.

¹⁵ Practical Bacteriology, Microbiology and Serum Therapy, Longmans, Green & Co., London, 1913.

¹⁶ Loc. cit.

¹⁷ Ztschr. f. Hyg. und Infektionskrank., xxxvii, 52.

body of the animal. The relation of streptococci to poliomyelitis cannot as yet be said to have received final interpretation, although the evidence for their being the primary exciting cause is but slight. Rosenow and Towne¹⁸ claim to have demonstrated that the small forms are derived from the larger diplococci by a double fission of the latter. The Berkefeld filtrates from paralytic monkeys have also been grown to the large forms by special methods. The evidence is chiefly morphological, and as yet is too incomplete to be in any way conclusive. They speak of "cycles of division," but in too casual a manner for one to consider that they regard the various forms as phases of bacterial life-cycles, physiologically speaking. Neither is the evidence sufficient for regarding the small forms as identical with the organism of Flexner and Noguchi. The findings are sufficiently suggestive to merit more study, paralleling as they do some of the above-related ones. Rosenow has suggested a relation between them and what is evidently the causative virus, but its purely morphological basis makes it entirely a matter of conjecture.

Tummcliffe¹⁹ has isolated a filtrable organism quite constantly from the early stages of measles, which can later be cultivated as a diplococcus and toward which the serum later in the disease shows immune reactions, but here, again, final interpretation is not yet warrantable. It will not avail to further multiply such examples if I assume that the object of their citation has been made clear.

CONCLUSIONS. Recent studies into the etiology of disease have made necessary a reëxamination of the theories of bacterial pleomorphism and involution. An abandonment of the terms is not advocated, inasmuch as they are doubtless applicable to truly degenerative changes. If they have been misapplied to changes of a phasic nature it is obvious that the latter should receive a representative designation and for other reasons than purely academic ones.

A modified interpretation of these morphological changes may result in the reconciliation of many diverse factors associated with infectious diseases of both known and unknown etiology.

If there exist stages of bacterial life, in the sense depicted here, there necessarily must occur a reevaluation of the term "secondary invader." If we eventually regard as "genuine secondary invaders," those having definite stage relationship with the primary exciting bacterial cause of the disease, the designation will be of greatest service in the investigation of diseases of unproved origin. The idea of genuine secondary invaders should also embrace the fact of the rather constant association of a certain type of organism with certain diseases.

¹⁸ Jour. Med. Research, vol. xxxvi, pp. 175-186.

¹⁹ Jour. Infect. Dis., 1918, xxii, 462; Jour. Am. Med. Assn., July 13, 1918, p. 104.

A NEPHRITIC DIET SHEET.

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AND

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THE diet sheet given below has been found useful and convenient in regulating the protein intake of nephritic patients. The physician often has a rather definite idea of how much protein it is advisable for a patient of this class to take—or rather not to exceed—without, however, any definite idea of how to tell him just what foods and what quantities he should eat. The usual way is to advise him to take so many eggs and so much milk; or we have elaborate menus, different for each day, with a varied but precise order of dishes for each meal. With this last scheme few private households are able to cope for any length of time. Moreover, it is important that restrictions shall not be excessive and that these patients receive sufficient protein in so far as their condition permits. With this sheet we believe we can make patients readily understand a method which they can easily carry out, whereby they receive, approximately speaking, the amount of protein we think they should have and no more.

In this sheet the ordinary articles of diet have been divided into three groups: The patient is instructed that whatever foods or dishes (in the current bill of fare where he happens to be) he may wish to eat he must first find on the sheet and take only in the quantities designated as full or half-portions. He is told that if the article is found in Group I a full portion counts 1 in the score for the day; if it is found in Group II it counts 2; he must keep count and "make" the total score prescribed for him. Now the quantity of each article given on the sheet as a full portion contains approximately 4 grams of protein in Group I and 8 grams in Group II. We divide the number of grams of protein we wish the patient to have in a day by 4, and the result is the figure we must write in (in the blank space left for the purpose) to represent what his daily score should be. The protein in the portions in Group II is, of course, twice as much as that contained in those of Group I; therefore a portion or helping of a food listed in Group II scores 2 while those of Group I count but 1. Group III lists foods of so low a protein content as to be negligible. It goes without saying that foods not found on our sheet may be easily added to it. The foodstuffs listed have been selected and grouped merely on the basis of the protein content. We doubt that any of these foods are

The sheet will probably be of the greatest usefulness in the so-called out-patient "classes," at which its meaning and use can be explained to groups of patients. One change might be made in the direction of greater simplicity. It will be seen that the size of the portions of fish and meats is a little different for each kind, but all are close to two cubic inches. It would perhaps be better to have a uniform portion for all meat and fish, that is, the lean part of a lamb chop or a piece 2" x 1" x 1". This is an amount easily visualized, and a block of wood could even be cut in the requisite dimensions and shown as an object lesson.

With the varied diet which the patient will naturally choose for himself under this system he will usually get sufficient calories for his needs. That this is so will be discovered if he is told at intervals to bring in a list of the foods he has eaten on two or three days previous. When, however, his protein has been cut down to the neighborhood of 30 grams a day it may well be found that he is not getting calories enough. If so a definite daily amount of butter, cream, olive oil and sugar can be prescribed, with instructions to take them on his other food. For convenience of estimation, on the physician's own sheet the calories may be written in after each portion.

Finally, this scheme, as will be readily apparent, is based essentially on the diet chart published years ago by Arnold, which in the opinion of the writers should have met with a more general use than so far as they know, has been the case.¹ It was Arnold's great merit to point out that uniform amounts of protein can be taken by common measures in quantities of food which are about what one would naturally take as a serving. Arnold's charts, however, as we think anyone who has used them will agree, are of more service to the physician than to the patient. The scheme submitted herewith makes the data available as a guide for the patient and the physician.

We gratefully acknowledge the assistance of Miss Katharine Mitchell, formerly assistant dietitian at the Peter Bent Brigham Hospital.

ANTIPNEUMOCOCCUS SERUM (KYES'S) IN THE TREATMENT OF PNEUMONIA.¹

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IN 1911, Kyes² announced that he had succeeded in producing an antipneumococcus serum with high antibody content by a new

¹ Arnold, H. D.: Boston Med. and Surg. Jour., 1909, clxi, 457. Medical Communication, Massachusetts Medical Society, 1909, xxi, 631. Tr. Am. Climat. Assn., Philadelphia, 1909, xxv, 128.

² Read at the meeting of the Tristate District Medical Society (Wisconsin, Illinois and Iowa), Rockford, Ill., September 5, 1919.

² Jour. Am. Med. Assn., June 24, 1911, No. 25, lvi, 1878-1881.

method. The novelty lay in using an insusceptible host, the ordinary barnyard fowl, which circumstance allowed the use of unusually large numbers of virulent living pneumococci as antigen. It was, of course, a well-known fact in immunology that pathogenic antigen was not necessary for the production of specific antibodies, but this knowledge had not been applied in the production of antibacterial sera.

The above announcement was made after laboratory experiments, both *in vitro* and *in vivo*, had demonstrated high antibody content in the serum and its protective action in laboratory animals, as detailed by the investigator in his original paper. The next step was to determine its therapeutic value in man.

Extensive therapeutic testing is the final proof of the value of any curative serum. This truism applies with equal force to antitoxin and to antibacterial sera. In the case of the former, however, there is the additional certainty that one is dealing with a definitely standardized product, checked against known lethal doses of toxin, and this certainty is felt by the investigator both during the experimental work in the laboratory and in subsequent therapeutic testing. With a standardized product it is to be expected that definite results can be repeated. In the case of antibacterial sera, on the other hand, no accurate method of biological standardization has been devised. Protection against living organisms of varying virulence, rather than against known lethal doses of toxin, carries less conviction during the laboratory stage of investigation and makes therapeutic testing of even greater relative importance. The present report is made in this spirit. It is proper to state also that Kyes has not allowed control of production of the serum to pass from his hands pending such therapeutic testing, and that he still considers the serum in the experimental stage.

In 1918 Kyes³ published the results of the use of his serum in the treatment of 115 cases of lobar pneumonia, controlled by a series of 538 cases, in which serum was not used, but otherwise treated under the same conditions, and during the same period of time. The mortality in the serum-treated cases was 20.8 per cent.; in the control cases, 45.3 per cent.

The next therapeutic test to which the serum was put in any large number of cases was at the Base Hospital, Camp Grant, Ill. An account of its use in the treatment of 322 cases between October 1, 1917, and September 20, 1918, has been published recently.⁴ The death-rate was 7.7 per cent. While there were no control cases it was evident to the clinicians administering the serum that it had marked therapeutic value. In addition the series gave valuable

³ Jour. Med. Res., July, 1918, No. 3, xxxviii, new series; No. 3, xxxiii, 495-501.

⁴ McClellan, John H.: Jour. Am. Med. Assn., June 28, 1919, No. 26, lxxii, 1884-1885.

data concerning dosage and methods of administration and other clinical phenomena, and afforded opportunity to improve the serum further on the basis of therapeutic use. With the present report the above constituted a complete record of the use of the serum in pneumococcus pneumonia at this Base Hospital. Mention may be made also, for sake of completeness, of five recoveries from pneumococcus meningitis during the epidemic following combined intraspinal and intravenous administration of the serum.⁵

The present publication carries the record on from September 20, 1918, to May 1, 1919. It is properly divided into the epidemic period, during which it was possible to compare results in cases treated with and without the serum, and the period from the close of the epidemic until May 1, 1919, during which all cases received serum treatment.

There was very little question at Camp Grant as to the character of the infection with which we were dealing during the epidemic. The preponderating organism obtained by swab culture from the nose and throat, and by culture from the sputum, during the stage of so-called influenza, was determined after a very few days to be an organism of unusual virulence, conforming in all laboratory characteristics to the pneumococcus. The Pfeiffer bacillus was found in only a negligible number of cases. Pneumococci were obtained in pure culture, or preponderatingly, from the heart blood and organs of cases dead from pneumonia and from other forms of pneumococcus disease in a large proportion of the 198 autopsies done during the epidemic period.⁶ It seemed to us that no doubt could arise as to the causative organism either in the cases of so-called influenza or of pneumonia, and that in the virulence of the organism was to be found sufficient explanation of the type of pneumonia resulting. It was presumed, therefore, that treatment with serum would demonstrate therapeutic efficiency.

Since it is proposed to compare the mortality-rates in two groups of cases, those treated with and those treated without serum, the conditions under which the serum was administered should be noted. There was no preparation for control comparison. The serum had been used routinely in the hospital and the propriety of withholding an agent of presumed therapeutic value from any cases for purposes of comparison was considered doubtful under the circumstances. But when it became apparent that there would shortly be more cases of pneumonia than serum could be furnished for, it was decided to restrict its use to cases in a single ward for ease of administration

⁵ Litchfield, L.: Jour. Am. Med. Assn., May 10, 1919, No. 19, lxxii, 1345-1348.

⁶ Hirsch, Edwin F., and McKinney, Marion: Epidemic of Bronchopneumonia at Camp Grant, Ill., a preliminary report, Jour. Am. Med. Assn., November 21, 1918, lxxi, 1735-1736; and an Epidemic of Pneumococcus Bronchopneumonia, Jour. Infect. Dis., June, 1919, No. 6, xxiv, 494, 517.

until more serum should become available. Its use was extended later to a second ward. Cases were admitted to these wards as fast as vacancies occurred, either directly from the receiving office or by transfer from so-called influenza wards by other individuals than those interested in or responsible for the treatment. There was therefore no possible selection of favorable cases. These wards were equipped in no essential way differently from the other pneumonia wards in the hospital. The serum was withheld from no cases in these wards. Finally, all deaths in the serum-treated group, except six that were determined*at autopsy to have been due to streptococcus pneumonia, were charged against the serum, in spite of complications or accompanying diseases which might have contributed to or have actually caused death, and regardless of the length of the time between serum treatment and the time of death. Four cases admitted between September 26 and 30 died in November; two admitted September 26 died in December; one admitted September 30 died the following February.

Another circumstance especially unfavorable to the serum record should be explained. On October 1 it was decided to rearrange cases in three contiguous wards, transferring all acutely sick cases in Wards 12 and 13 to Ward 11, putting cases of apparently good prognosis into Ward 12, and convalescent cases into Ward 13. Ward 11 thereafter was to be the receiving ward for the group of three, from which patients were to progress as they improved. This was to protect patients moderately sick and conscious of their surroundings from the sight and sound of the dying. The same plan was put into operation in another group of wards a few days later, where the serum, which had now become available in larger quantity, was being used. It was proposed to extend the plan to the entire hospital, but the epidemic soon became so overwhelming that it was not carried further. Carried on in these two groups of wards without any thought of its effect on the serum record, for the serum was given to all cases admitted and transferred to these receiving wards irrespective of the stage of the disease, it is fair to state that the mortality was especially high among these transferred cases. However, these statements are not made as a basis for altering the death-rate of the serum-treated cases, and no figures have been compiled to show what might have been the death-rate if the serum had been administered to all cases on diagnosis. They are made to emphasize the fact that the circumstances were in no way made favorable for the serum-treated cases.

During the epidemic period 234 cases of pneumococcus pneumonia were treated with the serum. The number of deaths in this group was 39, a death-rate of 16.7 per cent. During the same period a total of 2064 diagnoses of pneumonia were made in the hospital. There was a total of 1088 deaths. The death-rate was approximately

52.7 per cent., but the total number of diagnoses and the total number of deaths include serum-treated cases and streptococcus cases, which must be subtracted for the purpose of this comparison.

Hirsch and McKinney,⁷ in a paper previously referred to, detailed the bacteriology found at 198 autopsies during the epidemic. Streptococci were found in a small percentage. It was apparent that clinical differentiation between streptococcus and pneumococcus pneumonia had been largely impossible during the epidemic, partly because of the type of the epidemic diseases and partly because the necessary laboratory investigation for such a large number of individual cases was clearly out of the question. The total number of diagnoses of pneumococcus pneumonia recorded in the hospital, therefore, included a certain number of streptococcus cases. But since six deaths are cut out of the list of serum-treated cases because it was determined at autopsy that streptococci were the primary invading organisms, it becomes necessary to estimate a fair reduction in deaths among cases not treated with serum, few of these cases having come to autopsy. Using the same proportion as obtained in the serum-treated cases it is estimated that 140 deaths due to streptococcus pneumonia occurred among the cases not treated with serum. With the figures thus obtained the mortality in these cases, as detailed in the accompanying tabulation, is figured to have been 53.6 per cent.

The comparison I wish to submit, therefore, is a mortality of 16.7 per cent. in 234 serum-treated cases of pneumococcus pneumonia, with a mortality of 53.6 per cent. in 1684 similar cases treated in other respects by the same methods except that they received no serum. In other words the death-rate in the serum-treated cases was somewhat less than one-third that in the cases compared.

The serum was administered intravenously in all cases. Shortly before the epidemic the dose was increased from 2.5 c.c. once or twice daily to 5 to 10 c.c. twice daily, and this larger dosage was maintained during the epidemic. In a few cases as much as 30 c.c. was given daily. Commonly a total of 60 to 90 c.c. was given in cases that recovered.

As to the clinical phenomena following use of the serum little more can be said than is told in the reduction of mortality. No marked changes were regularly seen after serum administration that were not seen in individual cases not treated with serum. It was the feeling of the writer, therefore, that any attempt to tabulate symptomatic changes in the serum-treated cases for comparison with control cases would bring personal impressions into the record to such an extent that any conclusions arrived at would be open to question. Reduction of mortality, however, is a definite phenomenon. Thera-

⁷ An Epidemic of Pneumococcus-Broncho-Pneumonia, *Jour. Infect. Dis.*, June 1919, No. 6, xxiv, 594-617.

peutic value of any treatment must finally be judged by this end-result.

The *modus operandi* of the serum is, of course, of great interest but except for the fact that the serum is antibacterial any statement would be purely hypothetical. As to the so-called foreign protein reaction it should be stated that in only approximately 5 per cent. of cases was there any appreciable reaction following the serum used during the epidemic. This non-specific reaction cannot, therefore, be considered a factor in the reduction of mortality.

Following the epidemic, cases of pneumonia were atypical. Streptococcus pneumonia was much more common than during the epidemic. But pneumococcus pneumonia itself was also atypical, conforming in symptomatology neither to lobar pneumonia nor to the epidemic bronchopneumonic type, though the appearance of the lungs at autopsy was more clearly that of the latter. There was evidence that the organism was dropping in virulence (unpublished observation of E. F. Hirsch). Finally, in March and April, 1919, lobar pneumonia began to reappear. During the period, therefore, from the close of the epidemic to May, 1919, when this record closes, there was a continually changing picture of disease in the pneumonia wards. It was difficult to establish a clinical standard of differentiation of streptococcus from pneumococcus cases.

But while this period was in many ways an unsatisfactory one in which to attempt to evaluate the therapeutic effect of the serum, not only because of lack of controls but also because of the facts above set forth, it is believed that the final compilation of pneumococcus cases was accurate and that the low mortality is credited properly to the serum. There were 5 deaths among 118 serum-treated pneumococcus cases, a death-rate of 4.3 per cent.

The record of the use of Kyes's antipneumococcus serum at Camp Grant can now be summed up. 322 cases of pneumonia were treated between October 1, 1917, and September 20, 1918, with a death-rate of 7.7 per cent.; these were cases of typical lobar pneumonia. 234 cases of epidemic pneumococcus-broncho-pneumonia were treated between September 21 and November 4, 1918, with a death-rate of 16.7 per cent. which is to be compared with a death-rate of 53.6 per cent. in 1684 control cases. 118 cases were treated between November 5, 1918, and May 1, 1919, with a death-rate of 4.3 per cent.; these were atypical cases of pneumococcus pneumonia, which seemed to indicate a gradual change from the epidemic type of disease back to the type of lobar pneumonia, probably due to a falling virulence in the organism. In addition 11 cases of pneumococcus meningitis were treated, with 5 recoveries, 1 fatal case having occurred since the publication by Litchfield (*loc. cit.*)

EPIDEMIC STATISTICS, SEPTEMBER 20 TO NOVEMBER 5, 1918.

Total number of diagnoses	2064
Total deaths	1088
Death-rate	52.7%
Serum-treated cases	240
Streptococcus deaths subtracted	6
Pneumococcus cases	234
Pneumococcus deaths	39
Death-rate	16.7%
Non-serum cases	1824
Streptococcus deaths, subtracted (estimated)	140
Pneumococcus cases	1684
Pneumococcus deaths (see below)	903
Death-rate	53.6%
Total deaths	1088
Serum deaths	45
Non-serum deaths	1043
Streptococcus non-serum deaths (estimated)	140
Pneumococcus non-serum deaths (see above)	903

INCIDENCE, ASSOCIATED PATHOLOGY AND CLINICAL DIAGNOSIS OF CHRONIC PERICARDIAL ADHESIONS.

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THE report of this investigation deals with a condition which, during the years recent and long passed, has received deliberate study from some of the most noted clinicians and pathologists, while apparently being seriously neglected by others equally noted. I refer to that pathological state characterized by an obliteration of the pericardial cavity, completely or in part, by adhesions. Associated with this there may or may not be extrapericardial adhesions. Because the adhesions associated with a pleural tuberculosis have a distinct clinical picture peculiar to this type of adhesions, we have sought, in so far as we were able, to exclude all cases possibly tuberculous from the series.

Since the study of this subject has been pursued only along lines of my own personal choice, no reference will be made to the not voluminous but rich and select literature. To the writer the two most perplexing features of this pathological state are its etiology and diagnosis. Many other intricate and interesting features surely do exist and will receive in their turn some discussion in which we may suggest that these associated features either explain the etiology or assist in rendering a diagnosis.

In the analysis here presented no definite theory as to the etiology will be advanced, as, even after a rather critical survey of the past histories of the cases representing this series, no specific etiology

could be exposed. A study of the etiology is so clearly interwoven with the associated pathology that it must be considered with the greatest advantage in association with the pathology found not only within the heart wall but within other organs as well. This clinical and pathological report is the result of the study of 30 cases of pericardial adhesions of various grades occurring in 514 consecutive autopsies at the St. Louis City Hospital. When all grades of adhesions are included there is an incidence of 5.8 per cent. represented in this series. For convenience of comparative study these cases were grouped arbitrarily into three classes: mild, moderate and extensive. From both a pathological and clinical point this arbitrary grouping is deceptive, in that it neglects the position of the adhesions which at least almost certainly determines the presence or absence of clinical signs as well as their severity when present. When classified in this manner, however, the 30 cases were grouped as: mild adhesions, 4 cases; moderate adhesions, 18 cases; extensive adhesions, 8 cases. Extensive was reserved for those cases in which the pericardial cavity was completely obliterated. In some of these cases there were also extrapericardial adhesions fixing the pericardium to the diaphragm, costal cartilages, pleura and lung or to the structures in the posterior mediastinum.

Adopting this classification reveals that of the 514 patients coming to autopsy 1.5 per cent. had extensive adhesions, 3.5 per cent. moderate adhesions and 0.8 per cent. mild adhesions. Unless the adhesions in the mild and moderate cases are almost selectively located, and especially if there are no extrapericardial adhesions, there is much doubt to be entertained as to the possibility of clinical recognition. The clinical diagnosis of the extensive adhesions seems to be assured, more especially, if there are extrapericardial adhesions of moment present.

The apparent causes of death in the 8 cases of extensive adhesions were:

Typhoid fever	3 cases
Acute endocarditis	1 "
Operation for the relief of adhesions	1 "
Carcinoma of stomach	1 "
Chronic nephritis	2 "

The apparent causes of death in the 18 cases of moderate adhesions were:

Cerebral apoplexy	2 cases
Carcinoma of liver	1 "
Carcinoma of stomach	1 "
Acute nephritis	11 "
Pulmonary tuberculosis	1 "

In the mild cases 2 died of cirrhosis of the liver and 2 from chronic nephritis.

A feature relative to the apparent cause of death is the fact that 50 per cent. of the series died from chronic nephritis, presenting apparently a possible relationship between the etiology of chronic nephritis and pericardial adhesions. In fact this is true not only of chronic nephritis but of associated pathological changes in numerous other organs. In this light a careful study of the pathology present in other organs besides the pericardium would establish somewhat the nature of the etiology at least in some general way. In the 30 cases of this series the associated changes found in the lungs and pleura were as follows:

Pleural effusion	3 cases
Chronic pulmonary tuberculosis	6 "
Chronic pleural adhesions	15 "
Chronic passive congestion	18 "

The associated changes within the heart and large vessels were:

Chronic myocardial fibrosis	15 cases
Acute endocarditis	1 "
Chronic arteriosclerosis	14 "
Chronic endocarditis	6 "

Within the entire series only one heart presented no marked changes. In this case the adhesions were termed moderate. In the liver were the following associated changes:

Chronic passive congestion	14 cases
Chronic cirrhosis	10 "
Chronic degeneration	8 "
Chronic perihepatitis	3 "
Hepatic syphilis	2 "
Livers presenting no marked changes	1 "

The spleens presented the following changes:

Chronic passive congestion	20 cases
Chronic perisplenitis	2 "
Chronic hyperplasia	2 "
Chronic atrophy	1 "
Spleens presenting no changes	5 "

The associated findings in the kidneys were in the majority of cases very extensive. The following changes were found:

Chronic nephritis	24 cases
Chronic congestion	3 "
Acute cloudy swelling	3 "
Amyloid degeneration	2 "

There were no kidneys free from pathological changes.

At once in this study one is impressed with the frequency of pericardial adhesions associated with myocardial, vascular, hepatic and renal changes, for the most part fibrotic in type. The most natural supposition is that a common etiology exists in the form of a chronic infection or intoxication. This conclusion is contrary

to those placing the pulmonary, hepatic and renal changes secondary to the pericardial state because of the accompanying cardiac insufficiency. This is also supported by the results of some experimental work of the writer, which will be published later.

From the standpoint of etiology, pericardial adhesions seem to fall into three classes: (1) The tuberculous which we do not desire to discuss; (2) those resulting from an attack of acute pericarditis or more probably pancarditis secondary to or complicating some acute infectious disease as rheumatic fever, tonsillitis, lobar pneumonia, typhoid, etc. Here the acute pericarditis may or may not result in an effusion. Following this acute stage there usually develop fibrous adhesions, not only within the pericardial cavity, but, more important, adhesions between the pericardium and the anterior chest wall, the pleura, diaphragm or the structures within the mediastinum. This class is the one most easily recognized clinically, not only because of the extent but the nature and location of the adhesion.

The third class includes those cases which give no history of previous acute infections of any kind. This class present adhesions of all grades, mild, moderate or extensive. The adhesions being located at various places within the pericardium and uniting the pericardium with various extrapericardial structures. At times the adhesions are of no clinical importance while at other times they assume a position of immense importance because of the associated cardiac insufficiency and because of the prognosis of certain acute infections in patients suffering with this cardiac insufficiency. The adhesions in this class are probably the result of long and continued injury to the pericardium from chronic infections or some unknown intoxication. In this class we see most typically the associated chronic changes in the liver and kidneys.

In general, this class presents clinical symptoms and physical findings leading to a suspicion or diagnosis of adherent pericardium at a later age than the foregoing class, because the foregoing class is the result of acute infections usually acquired in childhood or early adult life and the cardiac symptoms appear a few years later. The formation of the adhesions in class three is insidious, resulting in cardiac symptoms years later. Unless the adhesions are selectively located, or else are very extensive, the clinical recognition is not only impossible but unimportant. When the adhesions are so placed as to interfere gravely with the cardiac function or are extensive the clinical recognition is important because of the cardiac insufficiency and because of the influence of this insufficiency upon the prognosis of certain acute infections, notably pneumonia and typhoid fever.

The signs present in any case of adherent pericardium will depend upon the efficiency of the heart toward maintaining a normal circulation and upon the location of the adhesions.

For the purpose of a concise delineation of the signs which may possibly lead to a recognition of this pathological state, we may resort to the classical rescription of the signs recognizable by inspection, palpation, percussion and auscultation.

Inspection: A patient suffering with adherent pericardium which has so disarranged the cardiac efficiency as to produce symptoms, presents about the same general symptoms as are common to all cases of cardiac decompensation.

In addition to these general symptoms we frequently are able to see the veins of the neck and face especially full during inspiration, while during expiration the veins collapse. The sign first described by Friedrich was supposed to be of some value in the diagnosis of pericardial adhesions. It is present, however, wherever there is a weakness of the right heart from any cause. Probably the most valuable sign to be noted upon inspection is a distinct retraction of the lower end of the sternum and the costal cartilages synchronous with cardiac systole. This results from adhesions between either ventricle and the pericardium at or near the attachment of the latter to the diaphragm. The retractions will be more distinct upon the side corresponding to the ventricle most densely adhered. The retractions will also be greater if in addition to the ventriculopericardial adhesions there are present phrenopericardial adhesions obliterating the normal phrenopericardial angle. At times these extrapericardial adhesions can be definitely demonstrated by carefully taken stereoscopic plates. The retraction of the costal arch may extend posteriorly to the eleventh or twelfth rib. There should, as Broadbent has observed, be a definite retraction of the costal arches and not merely of the interspaces, as a recession of the interspaces alone may be due to atmospheric pressure associated with extensive cardiac hypertrophy. When there are adhesions between the pericardium and the parietal pleura associated with obliteration of the pericardial cavity adjacent to either ventricle there will be seen systolic retractions of the costal cartilages or interspaces overlying the heart. Upon several occasions the writer has seen the sternum, costal arches and interspaces under prominent systolic retractions where there existed extensive pericardial and extrapericardial adhesions.

A retraction of the interspaces alone over the precordium is frequently seen to result from extensive cardiac hypertrophy; the retractions being near the sternum in right ventricular hypertrophy, and at or near the apex when the hypertrophy is of the left ventricle. Unless borne in mind these retractions might be considered as indicative of pleuropericardial adhesions.

In the study of this series, palpation was of only limited value. The diastolic shock so frequently described over the precordium was absent in a great majority of the cases. When present and distinct it may indicate the presence of rather dense adhesions

about the roots of the great vessels. Of more value apparently is an otherwise unexplainable absence of the impulse, or in the presence of a palpable apex impulse the failure of this impulse to change position corresponding with the change in the position of the body.

Anyone devoting close study to the physical phenomena of pericardial adhesions, surely is impressed with the value of carefully conducted percussion in the clinical recognition of these cases. The left border of cardiac dullness normally changes about 3 cm. with the change from the right-lateral to the left-lateral position. Likewise there is a change of 3 cm. in the lung border over the precordium during deep respiration. If either of these normal phenomena is absent, and its absence not explained by some extrapericardial condition, it remains a strong indication of pericardial adhesions. An absence of a change in the position of the cardiac dullness is present even without extrapericardial adhesions, while the fixation of the lung borders occurs only in the presence of pleuropericardial adhesions.

Auscultation reveals nothing distinctive of adherent pericardium. There may be various murmurs indicating the presence of an associated valvular disease, possibly the result of an inflammatory process responsible also for the pericardial adhesions, meaning, of course, that there existed at one time a pancarditis. This is usually the result of acute rheumatic infection.

The presystolic rumble and reduplication of the first sound are in no way distinctive. There remain certain accessory signs, some of which are present in certain cases, and while not absolutely diagnostic, are of great corroborative value.

Cooper's paradoxical respiratory ratio is of distinct value, but being present also in other conditions, it is only of great assistance if pronounced.

Riess's gastric sounds, whereby the heart sounds assume a loud and metallic quality, when heard over the epigastrium are apparently present when the adhesions are very extensive and involve the diaphragm.

There has been a syndrome described by Pick which today bears his as well as numerous other names, whereby there is chronic pericardial adhesions, chronic mediastinitis, capsular cirrhosis of the liver and chronic peritonitis with ascites. This syndrome has been considered by some as originating in the pericardium and because of the adhesions involving the inferior vena cava produce a passive congestion of the liver and other organs, and in this way account for the abdominal pathology. The pericardial, hepatic and peritoneal findings are quite probably independent and distinct, but the result of a common etiology as a chronic infection or intoxication. Most probably Pick's syndrome is nothing more than a very advanced type of adherent pericarditis described under class 3, the pathology being very extensive and pronounced.

In the diagnosis of adherent pericarditis most probably the greatest assistance comes from the recognition of well-defined cardiac decompensation, wherein there are no demonstrable valvular or myocardial changes to account for the decompensation. This should always arouse the suspicion of adherent pericarditis. Likewise a decompensating heart which reveals no abnormal findings relative to its size, shape and position should be investigated thoroughly for adhesions. Most probably if the physical examination as delineated above is conducted carefully, while bearing in mind the possibility of adherent pericardium, very few cases of extensive adhesions will be overlooked. I believe we have been able in some cases, especially when the adhesions obliterate the cardiophrenic angles or become dense in the mediastinum, to decide the diagnosis by means of carefully taken stereographic plates. When the adhesions are mild or moderate and not selectively located the diagnosis most probably is not only impossible but unimportant.

EFFECT OF THERAPEUTIC DOSES OF MERCURY ON THE KIDNEYS AND THE DURATION OF ITS EXCRETION.

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THE renal excretion of the mercurials, following their various methods of internal administration, has been the subject of frequent study in the past. Following their elaboration of a "New and More Delicate Test for the Detection of Mercury," Wile and Elliott were able to add materially to our knowledge of the drug's action, following its use in the form of injection and inunction. It has seemed, therefore, that a similar study of calomel following its internal administration might prove worthy of description. The scope of the experiment, as undertaken at this time, was limited to a calculation of the period of time over which the drug was excreted and a study of its action upon the kidney as determined by urinary findings.

The method for the detection of mercury employed in the experiment, in brief, embodies the use of copper dust in an acid solution of the suspected material. The mercury is taken up to the last trace by the copper dust. The latter is then collected, dried and heated in the distal end of a bulb tube. The mercury is thus vaporized and deposited as an amalgam in a small particle of gold leaf. By this method one-millionth of a grain of mercury in solution can be detected microscopically.

It was interesting to note that in establishing controls for the experiment many patients were found unsuitable for the reason that

they were not mercury-free. Inquiry revealed that the majority of these patients had received previous antisyphilitic treatment, entailing the use of mercury in one of its various forms. In the light of previous studies it is a well-known fact that mercury can be found for years in the urine of patients who have previously received the drug, so this finding was to be expected. Obviously these patients were rejected at once. Controls, finally, were selected from other clinics, each according to the following conditions: (1) Those that gave no history of previous mercurial ingestion must give one negative test for mercury in the urine; (2) if there were a history of previous mercury ingestion or if the patient had ever been exposed to mercurial vapors two successive negative tests over twenty-four-hour specimens were required.

In addition, each specimen of urine was subjected to a complete analysis to ascertain whether it was normal in other respects. Chemical and microscopic tests on a centrifuged specimen were required to be negative. A complete record of all analyses was preserved.

Having thus determined the standards the first application of the test was begun by the internal administration of calomel in the usual way: One-quarter-grain doses over fifteen-minute intervals. The conditions under which the experiment was made were: (1) No drastic saline or other purge should follow the ingestion of the mercury; (2) all specimens must be collected in mercury-free containers at various intervals; (3) only one course of the drug should be given. The various dosages that are most commonly given, therapeutically, were used in the experiment. The urines were then collected at the intervals shown in the tables and were subjected to the test for mercury as described above. The results were carefully tabulated.

SERIES I.—CALOMEL, GRAINS TWO IN ONE-QUARTER-GRAIN (DIVIDED)
DOSES AT FIFTEEN-MINUTE INTERVALS.

Patient.	6-hour.	12-hour.	24-hour.	2d day.	3d day.	4th day.	5th day.	6th day.
1	—	—	X	X	X	X	—	—
2	—	X	X	X	X	X	Patient left hospital	0
3	—	—	X	X	X	X	X—	—
4	—	X	X	X	X	X	X	X
5	X	X	X	X	X (X)	X (X)	—	—
6	—	X	X	X	X	X	—	—
7	—	—	X	X	X	X	—	—
8	X—	—	X	X	—	—	—	—

SERIES II.—CALOMEL, GRAINS ONE AND A HALF IN ONE-QUARTER-
GRAIN (DIVIDED) DOSES AS ABOVE.

Patient.	6-hour.	12-hour.	24-hour.	2d day.	3d day.	4th day.	5th day.	6th day.
1	—	—	—	X	X	X—	—	—
2	—	—	X	X	X	X	X	—
3	—	X	X	X	X (X)	—	—	—
4	—	—	X	X	X	X	—	—
5	—	X	X	X	X	—	—	—
6	X—	X	X	X	—	—	—	—
7	—	X	X	X	X	—	—	—

SERIES III.—CALOMEL, GRAIN ONE IN ONE-QUARTER-GRAIN DOSES AS ABOVE.

Patient.	6-hour.	12-hour.	24-hour.	2d day.	3d day.	4th day.	5th day.	6th day.
1 . . .	—	X	X	X	X	X	—	—
2 . . .	—	X	X	X	—	—	—	—
3 . . .	—	X—	—	X	—	—	—	—
4 . . .	—	X	X	X	—	—	—	—
5 . . .	—	X—	X	X	—	—	—	—

SERIES IV.—CALOMEL, GRAIN ONE-QUARTER, ONE-QUARTER-GRAIN DOSES.

Patient.	6-hour.	12-hour.	24-hour.	2d day.	3d day.	4th day.	5th day.	6th day.
1 . . .	—	X	X	X	—	—	—	—
2 . . .	—	X	X	X	X	—	—	—
3 . . .	—	X	X	X	X—	—	—	—
4 . . .	—	X	X	X	—	—	—	—

X=Urine showed hyaline casts and trace of albumin.

From these charts it can be seen that:

1. All cases showed a positive test for mercury on the second day.
2. There was a greater excretion of the drug on the second day than any other day.
3. The heaviest excretion of mercury was between the forty-second and the seventy-second hours.
4. Mercury was detected in some cases as early as the sixth hour and as late as the sixth day.

In addition to carrying out the method for detecting mercury in infinitesimal amounts in each urine, every specimen was carefully subjected to both chemical and microscopic tests for the presence of material that might suggest kidney changes. In all cases except those marked X the urine analysis was entirely negative. In the instances marked a trace of albumin and a few hyaline casts were found.

CONCLUSIONS. 1. The excretion of calomel in ordinary therapeutic doses begins within six to twelve hours and is continued until the sixth day, depending upon the size of the dose.

2. A small dose of the drug is excreted as rapidly as a larger dose, but over a shorter period of time.

3. In so far as could be determined by the urine analysis the drug is excreted without injurious effects upon the kidney.

I wish to thank Dr. Udo J. Wile for his invaluable criticisms and for checking over my results, as well as for the laboratory facilities which he placed at my disposal.

REVIEWS

THE MEDICAL ASPECTS OF MUSTARD-GAS POISONING. By ALDRED SCOTT WARTHIN, PH.D., M.D., Professor of Pathology and Director of the Pathological Laboratories of the University of Michigan, Ann Arbor, Michigan, and CARL VERNON WELLER, M.S., M.D., Assistant Professor of Pathology, University of Michigan, Ann Arbor, Michigan. Pp. 267; 156 original illustrations. St. Louis: C. V. Mosby Company.

DR. WARTHIN'S and Dr. Weller's monograph on *Mustard-gas Poisoning* represents a war research problem which was carried on very intensely during the period of the war. It represents an extremely complete and careful study of the medical aspects of gassing and various lesions produced by this gas and the treatment which should be employed in gassed patients. From an experimental and pathological standpoint the book is extremely complete. From a clinical standpoint, however, the book does not represent by any means a complete exposition of the subject. To those who are interested in the clinical aspect of gassing, the regimental and the base hospital surgeon, the particular applicability of the experimental work to the practical is not sufficiently dwelt upon. This applies particularly to the treatment of the pulmonary complications and lesions, and more especially the late results.

Those who have seen large numbers of cases of mustard-gas poisoning have found that the important outstanding lesions were in the skin and respiratory tract. The treatment of the skin lesions as outlined, seems entirely adequate; that of the respiratory tract is not so. Eye lesions were comparatively rare and only infrequently of much importance. Under eye injuries there is recommended the wearing of antidimming goggles. This suggestion is contrary to the advice of the ophthalmologists in the A. E. F. Dr. Warthin also reports a leukocytosis in gas cases, whereas Krumbhaar found that a leukopenia was quite constant, reaching its greatest intensity in the severe cases.

The monograph on this subject represents a really splendid piece of work. The slight criticism that has been expressed by no means reflects upon the excellence of the work. The authors' contribution to the study of this subject is a valuable addition to our knowledge of the effects of mustard-gas poisoning, and it will undoubtedly remain the authority on this subject for many years.

J. H. M., JR.

FACIAL NEURALGIA AND ITS TREATMENT. By J. HUTCHINSON, F.R.C.S., Surgeon to the London Hospital; Examiner in Surgery and late Hunterian Professor at the Royal College of Surgeons. Pp. 216; 37 figures. New York: William Wood & Co.

THIS book, the first in the language, deals with the various phases of trigeminal neuralgia, its types, etiology, pathology and treatment. To the author thanks are due for defining clearly the minor from the major form, two distinct diseases. To the major or epileptiform neuralgia, or "tic douloureux," the volume is chiefly devoted. Prevalent ignorance of the existence of a sure cure for the pain or the unfounded (unless from early statistics) belief that the operation will either kill or cause the loss of sight are largely responsible for the long abject misery of these patients, their frequent addiction to morphin and then to suicide.

The author laments the great delays these patients suffer before being brought for radical operation, the vicious extraction of sound teeth and miscellaneous, useless efforts to find a focus of infection, the employment of drugs (for true major neuralgia is related neither to syphilis, gout nor the rheumatic diathesis; in fact, its etiology is wholly unknown and spontaneous cure is unheard of); ligation of the common carotid artery, excision of the superior cervical ganglion or any of the peripheral operations, all of which are now obsolete. There are only two legitimate procedures: alcoholic injections of the main divisions or of the ganglion, which afford relief for about nine months, and operation on the Gasserian ganglion or its sensory root, which offers permanent cure.

The development of the major operation is traced, chief attention being paid to excision of the ganglion, but particularly to the author's operation, which removes only the outer two-thirds of the ganglion, leaving intact the ophthalmic division and its share of the ganglion, thereby preventing corneal ulceration and lessening the danger of wounding the cavernous sinus. It is unfortunate that Mr. Hutchinson has not acquainted himself more accurately with the American literature in recent years. He states (page 118) that the Spiller-Frazier operation is "more difficult, dangerous and uncertain" than his own method. As to danger, Hutchinson, 70 cases, 3 deaths, 4 per cent. mortality; Frazier, 129 cases, 1 death, 0.77 per cent. mortality. The rankest injustice to Americans is the publication of a full-page illustration (including the legend) of a woman with a depressed zygoma, an ugly, disfiguring scar on the temple and her eyelids on one side sewed together for corneal ulceration. The legend, in part, reads: "Showing site of flap incision for the Spiller-Frazier operation." He goes on to say that these are "the conditions which should be avoided." Frazier never resects the zygoma or cuts outside the hair

line. Lastly, Hutchinson refers to Cushing as doing an obsolete, complicated operation, which has removal of the ganglion as its goal, whereas he actually performs the Spiller-Frazier operation, which leaves the ganglion intact.

J. A.

ANAPHYLAXIS AND ANTI-ANAPHYLAXIS. By A. BESREDKA, Professor at the Pasteur Institute. English Edition by S. ROODHOUSE GLOYNE, M.D. (Leeds), D.P.H. (London), Pathologist to City of London Hospital for Diseases of the Chest, Victoria Park. Pp. 143. St. Louis: C. V. Mosby Company.

THE translation of this monograph has been undertaken for the purpose of presenting to the English-speaking public the work of Besredka on the subject of anaphylaxis which he had accomplished before the war started. The book is introduced to the reader by four different introductions, following which is a historical sketch of anaphylaxis. The three succeeding chapters dwell on the sensitizing injection, the toxic injection and the anti-anaphylactic (desensitization) injection. The next two chapters are on anaphylaxis in the presence of other substances, and theories relating to anaphylaxis. The last chapter is a summary by the translator of the recent work on anaphylaxis. This last chapter is by no means complete, nor can the translator be blamed entirely for that on account of the disruption of the mail service, publication, etc., during the war or immediately following it.

Besredka undoubtedly stands as the great authority on the subject of anaphylaxis. He believes that the phenomenon of anaphylaxis is produced by an antibody becoming attached to nerve cells, permitting the entrance of the antigen which suddenly penetrates them and producing the characteristic symptoms. He believes that there is no true anaphylatoxin.

The monograph presents the subject in a clear, precise manner. It will be of particular value to those who are interested in this subject, more especially to those who are giving therapeutic sera and vaccines.

J. H. M., JR.

SYPHILIS. By HENRY H. HAZEN, A.B., M.D., Georgetown University. First Edition. Pp. 647; 160 illustrations (16 in color). St. Louis: C. V. Mosby Company.

IT is the greatest pleasure to read a book that raises the subject of syphilis above the level of a chapter in genito-urinary diseases and places it on the wonderful medicine-wide plane to which it is entitled. This Dr. Hazen's book does, for he brings to us not only his own

well-known efforts in this field, but has collaborating with him such authorities as Major M. A. Reasoner on infection and immunity, Dr. John E. Lind on nervous system involvement, Colonel C. F. Craig on the Wassermann test, and Dr. Jay F. Schamberg on the arsenical preparations. Dr. Virginius Dabney and Dr. L. H. Greene have written on the ear and eye infection respectively. Dr. H. A. Fowler's contribution on syphilitic nephritis is a most important exposition, while the chapter on endocrine gland infection is a valuable addition, with probably the first correlation of this literature. It is a pity that under prophylaxis the author did not make the effort to incorporate the wonderful lesson the American Army taught in France, and one might likewise criticize the chapter on diagnosis as putting too much dependence on the Wassermann test, or, possibly better said, by omitting the exposition of the clinical diagnosis. The chapter on treatment leaves one thoroughly familiar with the various drugs at hand and their individual administration, but lacks the proper guide and exact advice as to when and how to use them. The book is written throughout in a uniform, easy style that is most readable and loses none of this charm under the handling of the various authors. Dr. Hazen has a most happy ability in introducing quotations from other writers, and strengthens his subject repeatedly by using in a most admirable way the teachings of other authorities that leaves with the reader the feeling that the ground has been completely covered and the last word has been said. The book is profusely and splendidly illustrated; it is published in a way that leaves nothing to be asked, and one of its most valuable adjuncts is the excellent bibliography that is appended to each chapter.

A. R.

DISEASES OF THE EAR, NOSE AND THROAT. By HERBERT TILLEY, Surgeon to the Ear and Throat Department, University College Hospital, London. Fourth edition. Pp. 844; 74 illustrations. London: H. K. Lewis & Co., Ltd.

THIS work, as it now appears in its fourth edition, is a very complete and excellent text-book on diseases of the nose and throat. Since the last edition, as the author states in his preface, so great an advance has been made in certain phases of rhinology and laryngology that it has been necessary to absolutely rewrite the chapters on frontal sinus suppuration, the technic of enucleation of the tonsils and the subject of endoscopy, and to add entirely new chapters on certain affections of the trachea and esophagus, intranasal operations on the lacrimal apparatus and the intranasal routes for operations on pituitary tumors.

On the whole the book gives one the impression of being based more on the author's great experience than on a searching review of

the world's literature, and while this in some ways gives the book a peculiar value, we believe that a larger use of the literature outside of his own country would make an international adoption of the book much more easy. In this connection it is interesting to note that the author describes very closely what we in this country are in the habit of calling the Sluder method of removing tonsils, and gives Drs. Whillis and Phybus, of Newcastle-upon-Tyne, the full credit of devising the operation. Likewise an almost identical instrument with the Laforce tonsillectome is called Elphick's guillotine. Very frequently we note with pleasure a very extensive and accurate knowledge of pathology and modern laboratory revelations, and though this showing is not consistent throughout the book, the laboratory aspect is fairly reliable; much more so than the average book on diseases of the nose and throat. The clinical and operative side is excellent, well illustrated and with clear, easily read text, and the number of both minor and major operations carefully described is quite amazing. The great value of the work lies in the thoroughness with which the author has covered his field, not skimping any part, but giving space enough to all subjects for sufficient detail to make the work a real text-book of the whole category of nose and throat ailments. G. B. W.

ANATOMICAL DIAGRAMS. FOR THE USE OF ART STUDENTS. By JAMES M. DUNLOP, A.R.C.A., Lecturer on Artistic Anatomy in the Glasgow School of Art. Fourth edition. Pp. 72; illustrations on each page. New York: The Macmillan Company.

By the use of colored diagram the author presents the osteology and myology of the human body. The aims are to show the part played by the skeleton in determining the external form and to illustrate the shape and arrangement of the various muscles, especially the subcutaneous ones. The fact that this is the fourth edition shows that art students find it useful in the studio.

W. H. F. A.

A LABORATORY OUTLINE OF EMBRYOLOGY, WITH SPECIAL REFERENCE TO THE CHICK AND THE PIG. By FRANK R. LILLIE, Professor of Embryology in the University of Chicago, and CARL R. MOORE, Instructor in Zoölogy in the University of Chicago. Revised edition. Pp. 66. Chicago: University of Chicago Press.

This is a small book in paper covers, containing directions for laboratory work in embryology as given to medical students in the university of Chicago. For over fifteen years this book with

various alterations, has been utilized continuously in classes, and the present form therefore represents a well-tried and standard course of instruction. In the experience of the authors it has been found preferable for the student to follow out the development of each organ-system separately, through several ages of embryos, than to study each stage of the embryo in its entirety.

W. H. F. A.

BACTERIOLOGY IN ABSTRACT. By A. B. WALLGREN, B.S., M.D., Assistant Professor of Biology, University of Pittsburgh. Second edition. Pp. 338. Pittsburgh, Pa.: Medical Abstract Publishing Co.

THE second edition of bacteriology in abstract has recently appeared. The amount of useful and helpful knowledge contained in so small a volume is surprising. All fields that larger textbooks deal with are gone into here; necessarily, of course, in only an outlined, sketchy way. The index is fairly complete. The book is all and more than its author claims for it, and should prove a very useful volume for the student.

H. F.

DISEASES OF CHILDREN. By JAMES BURNET, M.D., M.R.C.P. (Edin.), Physician for Diseases of Infancy to and Physician in Charge of the Welfare Clinic at the Marshall Street Dispensary, Edinburgh. Second edition. Pp. 416; 9 illustrations. Edinburgh: E. & S. Livingstone. New York: William Wood & Co.

ARRANGEMENT of chapters in this small volume differs somewhat from the usual custom followed in pediatric works. In the first two chapters the examination of sick children and points of difference between children and adults are briefly but well described. Next in order are diseases of the newborn. After a chapter on diseases of the respiratory system and one dealing with diseases of the circulatory system, infant-feeding occupies a number of pages. Here the author discusses only his personal beliefs. Contrary to most authorities he does not advocate the use of sugar as an addition to milk mixtures, nor does he think that barley water is an advantage. He states that it is a fallacy to suppose that infants lose weight if sugar is omitted. Briefly, then, when it is necessary to feed babies artificially he uses only dilution of cows' milk with water. Citrated whole milk has given him good results, and scalded milk he finds preferable to raw, sterilized or pasteurized milk. While this chapter makes interesting reading, it does not seem to the reviewer that it

can be strongly recommended to the student or general practitioner as a system of procedure. Space does not allow of further analysis. Suffice it then to say that the usual chapters on various subjects are to be found. These are necessarily brief, due to the small size of the book.

A. G. M.

THE AFTER-TREATMENT OF SURGICAL PATIENTS. By WILLARD BARTLETT, A.M., M.D., F.A.C.S., and Collaborators. Two Volumes. Pp. 1066; 434 original illustrations. St. Louis: C. V. Mosby Company, 1920.

THESE volumes are certain of a hearty welcome from English-speaking surgeons. Throughout they have two properties of singular merit: they are essentially practical and they are up to the minute. As to the little details of postoperative management, most surgeons, even in the larger cities, allow themselves to practice for all cases one or two methods of treatment that may have seemed to prove of magic value in some "prize" case or other; in minor conditions they are prone to neglect the experience of others and the set-back to intercommunication of ideas during the war has accentuated this. To offset it and to strengthen the foundation for the rational, effective cure of the surgical patient a systematic reading of this work, embracing the experience of a group of able surgeons who have drawn generously from the literature of America, England, France and the German-speaking countries is particularly timely and necessary. Necessary because such a reading cannot but impress the reader with the host of modern methods that simplify convalescence, add untold blessings to the comfort of the patient and not infrequently in themselves effect cure or save life, methods that have not yet entered widely into circulation or at least too vaguely to be heeded, or perhaps old methods undeservedly forgotten.

Much is devoted to the minor subjects: postoperative subjective symptoms, sleeplessness, hiccough, headache, backache, skin eruptions, urinary retention, feeding, etc. There are valuable chapters on shock, miscellaneous abdominal tragedies, the various postoperative infections, the treatment of wounds, two unusually suggestive chapters on massage, exercise and physiotherapy and a chapter on radium and roentgen rays in malignancy, which is deserving of the closest study. The follow-up idea is represented by an able chapter on the reconstruction of the patient and by a series of forms prepared by Stuart McGuire for the guidance of patients leaving his immediate care.

It is a work that includes the widest variety of subject-matter, much too wide for mention, and is a book for the hospital intern and surgeon rather than for the student of medicine.

With the exception of two or three contributors it is a product entirely of St. Louis men. Much of the first volume, which deals with general considerations, was written by O. F. McKittrick, and most of the second, dealing with regional surgery, by Williard G. Bartlett. The printing is good, the illustrations unusually pertinent and the index a real service. J. A. D.

PHYSICAL RECONSTRUCTION AND ORTHOPEDICS. By HARRY E. STEWART, M.D., Capt., Medical Corps, U. S. A., Division of Orthopedics; Attending Surgeon, New Haven Orthopedic Dispensary; Instructor in Medical and Orthopedic Gymnastics and Massage, New Haven Normal School of Gymnastics, etc. Pp. 240; 69 illustrations. New York: Paul B. Hoeber, 1920.

It has been the author's object to present in condensed form the main principles of orthopedics in the treatment of defects in childhood, war injuries and industrial accidents, laying stress upon the treatment by massage, exercise, physical, mechanical and electrical and other types of physiotherapy.

The methods advocated have been tried out and proved of advantage in the reconstruction of the wounded of our own and allied nations, and are adaptable to our civil and industrial problems of like nature.

The problems of exercise, baking, massage, vocational therapy, electrotherapy and hydrotherapy are discussed in detail.

The application of these various treatments for congenital defects, spinal curvatures, joint injuries and diseases, foot-strain, fractures and dislocations is described in detail also.

The work should be of great value to physicians, reconstruction aides, physical directors, orthopedic assistants and nurses, not only in the better understanding of their work, but in emphasizing the vital importance of this so long neglected field. E. L. E.

MEDICAL CLINICS OF NORTH AMERICA. Mayo Clinic Number, Volume III, No. 3, 1919. Boston Number, Volume III, No. 4, January, 1920. Philadelphia and London: W. B. Saunders Company, 1920.

THE Mayo Clinic number of this bi-monthly publication has an unusually large number of contributors, twenty-three of whom present some communication on medical or closely allied subjects. The majority of these are reports of cases which are used as a text

for a brief discussion of the subject suggested by the case. There is a certain uniform excellence about these papers, and it would hardly seem fair to pick out any for a special commendation or criticism. As one of the articles is by Dr. Kendall, a chemist and not a physician, it will not be unjust to the other contributors to say that it is especially interesting, recounting, as it does, the end results of the splendid research which has been carried out by him and by his collaborators on the thyroid gland at the Mayo Clinic in the last ten years.

The Boston number of the *Medical Clinics* contains seventeen contributions from members of the teaching staff of Harvard University. These articles are all very interesting and well worth critical reading and study. The articles of the Harvard men exhibit the best type of medical work and represent impressively the purpose for which these *Clinics* are published. They give authors an opportunity to describe unusual cases or to write on subjects which are for the most part protean, and yet which are matters that the average reader frequently does not have at his finger-tips and which it is to his decided advantage to review from time to time. Furthermore, they present the newer diagnostic methods, therapeutic progress and the recent advances in general in the studies of the conditions which the author is describing.

J. H. M., JR.

SURGICAL CLINICS OF CHICAGO. Bi-monthly Volume IV, No. 1.
Pp. 231; 83 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

THIS number of the *Clinics* well sustains the reputation held by this work in the past. The contributors are all in the foremost rank in their respective branches and have many times presented articles to the readers of medical or rather surgical literature.

Each article is a text in itself and invariably illustrates some important point in diagnosis or some novel, useful and essential list of surgical technic.

The great value acquired from the *Clinics* is due to the concrete knowledge obtained from the individual patient explained before you. The problem is presented and solved before the reader's eyes.

E. L. E.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Origin and Nature of Multiple Sclerosis.—MARINESCO (*Rev. Neurol.*, 1919, xxvi, 481) thinks multiple sclerosis should be investigated as an inflammatory process caused by an infectious agent. The lesions are inflammatory in character and the sclerosis is secondary. A *resume* of previous experimental work is given. The author injected the spinal fluid from two cases of multiple sclerosis into guinea-pigs by intraspinal, intracerebral and intraperitoneal routes. The two pigs which had had intracerebral injections showed motor difficulties. The fluid from their fourth ventricles contained spirochetes, unlike the treponema of syphilis. The work was not carried further.

An Interesting Spinal Syndrome Following Gunshot Wounds.—LITTIG (*Monatschr. f. Psychiat. u. Neurol.*, 1919, xlvi, 112) reports nine instances of a spinal-cord syndrome named by him monoplegia spinalis spastica superior. Briefly this consists of a high cervical cord lesion followed by a spastic paresis or paralysis of one arm. Occasionally there are sensory disturbances in the region of the ulnar side of the paretic arm. This syndrome is usually the end-result of many cord wounds, such as a diplegia, hemiplegia or Brown-Séguard symptom complex, but may be primary.

Renal Glycosuria.—ALLEN, WISHART and SMITH (*Arch. Int. Med.*, 1919, xxiv, 523) found three cases of renal diabetes among forty supposed diabetics at U. S. G. H. No. 9. The histories and detailed reports of the laboratory tests are given in the article. No instances of levulose,

pentose or glycuronic acid excretion were encountered. No clue as to etiology was found. The prognosis seems to be good, for in no case in the literature has injury resulted from the anomaly, and it has never been known to have ceased. In the instances reported sugar excretion and water excretion have behaved as independent functions. Increase of sugar output did not increase water output. The salient features of carbohydrate metabolism in the three cases and in nearly all of the genuine cases are: "(1) A tendency to glycosuria so strong that sugar freedom is possible only with stringent restriction of diet or actual fasting to such a degree that health would be seriously impaired by attempting to keep glycosuria absent, if, indeed, life were possible at all—the cases in this respect surpassing true diabetes except for very rare examples of extreme severity; (2) normal power of actual carbohydrate utilization, as manifested by 'paradoxical tolerance,' *i. e.*, though some process in the kidney or elsewhere causes the waste of a certain quantity of carbohydrate, and this quantity may increase with increased carbohydrate ingestion, yet the soundness of the assimilative function is shown by the ready utilization of the greater part of every starch or sugar intake, no matter how large; (3) though the blood-sugar level is subject to some variations the low values found in many cases, even after large starch or sugar ingestion, stand in contrast not only to the condition in diabetes but also to the hyperglycemia of normal persons after such feeding." The authors lay emphasis on the desirability of ascertaining in each instance the nature of the reducing substance present in the urine obtained as soon as possible after leaving the kidney.

Exophthalmic Goitre, Basal Metabolism In.—MEANS and AUB (*Arch. Int. Med.*, 1919, xxiv, 638) have followed many patients with exophthalmic goitres over several years and have been able to observe the results of various forms of treatment. The method of approaching the results is based on the study of the basal metabolism. Short abstracts of the clinical findings of the hyperthyroid patients are included. The other data are presented by tables. Patients with exophthalmic goitre were treated either by rest alone, quinine hydrobromide, roentgen ray or operation or by a combination of these methods. They conclude that "using the basal metabolism as an index of toxicity in exophthalmic goitre" the majority of patients show as good results after two or three years following roentgen-ray treatment as following surgical treatment. "The safest program for the treatment of exophthalmic goitre, as a whole, is the routine irradiation of thyroid and thymus glands, in all cases, with surgery held in reserve for patients who do not then do well. Surgery is contra-indicated with patients whose metabolism is rising in spite of complete rest in bed, and also in patients of the type with moderate tachycardia and great metabolism increase, except when they have previously had thyroid and thymus glands treated by roentgen ray." They also believe that basal metabolism determinations may be of differential diagnostic importance in certain border-line cases.

Entameba Histolytica, Report on the Treatment of; Infections.—GUNN and SAVAGE (*Jour. Royal Army Med. Corps*, London, 1919, xxxiii, 418) report the result of treatment in 383 cases at Alexandria,

The diagnosis was based on the presence of *entameba histolytica* in stools. The patients were in every stage of the disease, some being only cyst carriers, some having large tender livers with high fever. They recommend that acute cases be treated with 1 grain of emetine daily for twelve days, followed by 3 grains of emetin and bismuth iodide for fourteen days. If the condition is very severe when treatment is first begun, and may probably prove fatal if not rapidly brought under control, they recommend an intensive course of treatment of 1 grain emetin hypodermically daily in the morning and 2 or 3 grains of emetin-bismuth-iodide at night. The patient should be carefully watched while such large doses are being administered.

Lumbar Puncture in Brain and Subdural Abscess.—BARRIES (*Arch. f. Ohren, Nasen. u. Kehlsopf. h.*, 1919, civ, 66) discuss at length the cerebrospinal fluid changes in brain and subdural abscesses. These may be placed in four groups as follows: (1) The fluid is entirely negative in uncomplicated brain or subdural abscess and may remain so until death. (2) The fluid may be cloudy but sterile, later becoming cell-free, in instances showing minimal leptomeningitis. (3) The fluid may be cloudy and contain bacteria, later becoming sterile if there is an extensive leptomeningitis. (4) The fluid may be cloudy and contain bacteria in cases running the course of an acute purulent meningitis. The fluid obtained by lumbar puncture may be of considerable help in diagnosis and prognosis if examined repeatedly. Since, as shown in the groups above, favorable changes are common in the fluid as the disease progresses, a single lumbar puncture may give a wrong impression of the extent and gravity of the meningeal involvement. In certain instances the brain abscess proves fatal although the spinal fluid shows changes which the author calls benign. By repeated lumbar punctures it is possible to gain knowledge only of the extent and gravity of the meningeal changes secondary to a brain or subdural abscess.

Spirillosis Following a Traumatic Hemothorax (Spirillose Pleurale au Cours d'un Hemothorax Traumatique).—LANCEREAUX (*La presse méd.*, 1919, xxvii, 556) observed a soldier, wounded by a small piece of shell at the left base. The foreign body was near the heart and moved with its pulsation. There was a large hemothorax. On the sixth day 1500 c.c. of bloody fluid was removed from the left pleural cavity. The fluid was sterile. Tapped again and in the fluid there were many active spirilla seen by ultramicroscope and stained specimens showed spirilla. The patient recovered after three thoracenteses and 0.15 gm. novarsenobenzol intrapleurally.

Neurological Complications of Typhus (Les Complications Nerveuses du Typhus Exanthématique).—PAULIAN (*La presse méd.*, 1919, xxvii, 541). After about fourteen days' incubation slight chills occur and malaise, backache, headache and fever appear. The face is flushed. About the fifth day of fever the exanthema appears. Its character may vary, at first discrete, at times petechial or even purpuric. There is no relation between the fever, the exanthem and the clinical form of the disease. Delirium appears early. About the thirteenth day the fever begins to fall and remits completely by the fifteenth day. In the

severe types there is carpalgia, the eyes injected, rapid respirations, tachycardia, cyanosis, trismus, stiffness of the neck, Kernig's sign and at times hiccough—a very grave sign. Coma vigil is often present. A meningeal reaction is constant—from the first to the fourth day. Cerebrospinal fluid contains mainly lymphocytes; fourth to twelfth day mononuclears; twelfth to convalescence lymphocytes. Nervous complications of two types: (1) During disease and (2) during convalescence. These are, briefly, hemiplegias, nuclear and midbrain lesions, postfebrile confusional states, regressive cerebellar syndromes, myelitides, neuritis and polyneuritis.

Occurrence, Course and Prevention of Chronic Manganese Poisoning.—EDSALL, WILBUR, DRINKER (*Jour. Industrial Hygiene*, 1919, i, 183). Manganese poisoning occurs among workers handling MnO_2 in manufacture of Cl_2 ; in grinding of MnO_2 ; in mill employees who work in dust containing Mn as oxides and silicates. Diagnostic points are: exposure for three months; languor and drowsiness; expressionless face; monotonous voice; muscular twitching—fine or very gross—cramps and stiffness in calves; worse at night or after exertion; hyperreflexia; ankle and patellar clonus; retropulsion and propulsion; slopping gait. Sensation intact: urine, blood, cerebrospinal fluid; sphincters normal. After harm is done there is no treatment. Problem is one of prevention.

Patches of Deep Pigmentation of the Oral Mucous Membrane not Connected with Addison's Disease.—WEBER (*Quart. Jour. Med.*, 1919, xii, 404) reports a patient, aged fifty-seven years, a Hungarian Hebrew, with remarkable pigmentation of the buccal mucous membrane of the palate and lips. There was no pigmentation of the skin. Necropsy showed extensive miliary tuberculosis without involvement of the pancreas, pituitary or pineal body or either suprarenal. No cause for the pigmentation could be discovered. He concludes: "There is a certain group of cases in which pigmentation, not connected with Addison's disease, occurs in the mucous membrane of the mouth. The pigmentation is in the form of blackish spots and patches in the mucous membrane of the lips or cheeks and sometimes of other parts of the mouth. It is associated with pigmentation of the skin of the face, especially about the mouth and possibly of other parts of the body. It occurs in persons of dark complexion, perhaps especially in Roumanian Jews and in certain races such as Lascars. It is of unknown causation and seems in some cases to be of "physiological" or perhaps of atavistic origin. It may be analogous to the black patches often present in the oral mucous membrane of dogs and other animals. It appears to be allied to simple pigment nevi of the skin on the one hand and to freckles on the other. Jonathan Hutchinson was probably the first to call attention to this class of pigmentation, which perhaps should include various cases published by French authors under the headings "physiological pigmentation" and "racial pigmentation." The author has carefully reviewed the literature of the subject.

Recent Additions to Our Knowledge of Typhus: Acquisitions Récentes sur le Typhus Exanthématique.—FOURCADE (*La presse méd.*,

1919, xxvii, 548). In 1909 Ricketts found oval rods, at times biscuit-shaped, and polar staining in the lice fed on infected blood of humans and monkeys. Prowazek, in 1913, found them in lice in Serbia. In 1916 da Rocha Lima found the same in the gastro-intestinal epithelium of pediculosis vestimenti and called them Rickettsia Prowazeki. The morphology and tinctorial qualities are given in the text. The louse seems to be obligatory intermediate host. The patient can infect the louse only during the febrile period. The louse becomes contagious four days after its infecting repast. The disease can be transmitted to man, apes and guinea-pigs. One attack confers immunity. The reaction of Weil-Felix is of great diagnostic importance. The technic is that of Widal's reaction, using Bacillus proteus X 19 of Weil-Felix instead of the typhoid bacillus. The reaction is positive in 50 per cent. of cases in the third week and constant after defervescence. Often a titer of $\frac{1}{50000}$ is found. A titer of $\frac{1}{30}$ is diagnostic.

SURGERY

UNDER THE CHARGE OF

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The Condition of the Appendix in Five Hundred Laparotomies on Patients Representing No Symptoms of Appendicitis.—WILLIAMS and SLATER (*Ann. Surg.*, 1919, lxx, 535) report the results of their study of the appendiceal pathology met with in the course of the routine examination of the right iliac fossa during five hundred gynecological operations. About one-third of all women operated on for various pelvic conditions, show undiagnosed lesions of the appendix. In some instances these lesions are the result of extension of an inflammatory process to the appendix from the pelvic organs, but at least one woman in every five shows an appendix lesion without symptoms and without discoverable cause (so far as the pelvic organs are concerned). These lesions are nearly all chronic in nature and consist of the following types: (a) adhesions without change in the muscular or mucous coats, (b) chronic inflammatory changes in all the layers, (c) pericecal veils. The frequency of these lesions is of importance in its relation to two questions: (1) Are such undiagnosed lesions of the appendix the undiscovered cause of reflex symptoms elsewhere? (2) Is there such a clinical entity as chronic appendicitis, or are the symptoms usually ascribed to chronic appendix disease in reality due to some other condition? The writers are inclined to the latter view.

Penetrating Chest Wounds.—LEBOWITZ and NADLER (*Surg., Gynec. and Obst.*, 1919, xxix, 429) reports the results of 276 penetrating wounds

of the chest admitted to a base hospital in France. The observation of the average case was confined to a period extending from the sixth to the thirtieth day after injury. The mortality of penetrating chest wounds that reached the base was low (5.4 per cent.), due chiefly to sepsis, pocketed empyema, and associated injuries. These patients require treatment in special wards. Coöperation of internist, pathologist, roentgenologist, and surgeon is essential. Hemothorax is the commonest event in chest wounds. Early diagnosis of infection is the most important duty at the base. Thoracotomy for infected hemothorax is the most frequent surgical procedure at the base hospital. The Carrel-Dakin treatment for empyema gives good results. Primary intrathoracic operations with closure may be performed easily after injury, in properly selected cases, with no more danger than abdominal operations. Of 21 cases operated upon and closed, 9 remained sterile.

The Technique of Gall-bladder and Common-duct Surgery.—RICHTER (*Surg., Gynec. and Obst.*, 1919, xxix, 455) says that the technic of gall-tract surgery is in the process of becoming standardized. The cystic duct should be isolated before division to insure the safety of the common duct. In the large acutely distended gall-bladders the cystic duct is pushed backward and upward away from the operator. If in these cases the peritoneum, as it is reflected from the liver on to the gall-bladder, is incised enough to admit a finger, the gall-bladder can be peeled out of its bed. The release of the tense gall-bladder in this way will cause the fundus to push its way out of the incision, and the cystic duct becomes mobilized and more accessible. The cystic duct should, Richter believes, rarely be clamped with its vessels *in toto*. He considers it unnecessary to ligate the cystic duct close to the common duct, but one must avoid the careless ligation of the apex of the gall-bladder. The reflected peritoneal flaps from the gall-bladder should not be sutured over the denuded liver, but should merely be pressed against it. The position of the raw surface is such that massive adhesions to it are naturally objectionable. The gauze pack is a much more patent cause of adhesion than the raw surface *per se*. Andrews suggests dropping the omentum in between the liver and the duodenum as a method of minimizing adhesions. Though many operators close the abdomen without drainage, it is almost universally suggested that drainage should be instituted after cholecystectomy. Willis has reported a series of thirty-eight cholecystectomies with drainage, with one death. This can be done safely without excluding the stump of the cystic duct from the peritoneum. Richter considers it illogical to drain the common duct or leave a tube in it following choledochotomy, provided no obstructive lesion is left behind. It is an essential requirement in carrying out immediate suture that the common duct should be patent; that no stone in the ampulla, no partial closure of its orifice from a thickened muscle of Oddi, or chronic pancreatitis should be present.

A Case of Sarcoma of Stomach.—KOETTLITZ (*Arch. méd., Belg.*, 1919, lxxii, 136) says that sarcoma of the stomach merits especial attention because of the rare occurrence of the disease. The patient, a musician, aged twenty-one years, presented himself for consultation June 24, 1915. He had been suffering for one to two years from vague gastric distress,

which had become exaggerated the last forty days. His father died at fifty-one of probable gastric carcinoma and his grandmother died of the same disease. The sickness began with aqueous regurgitations about one hour after eating. Rarely he had vomiting. He gradually lost weight over a period of two years. There was tumor to the left of and above the umbilicus. There was achylia gastrica, plus a tumor not involving the pylorus or at least not obstructing its action. The patient refused operation for forty-five days. During the period he was under observation he had severe periods of diarrhea. At operation there was found a large inoperable tumor in the pyloric region, involving also the pancreas. There was a chylous ascites present. The pathological report of a nodule was fibrosarcoma. He compares his case with Gosset's compilation in 1912 of 171 cases.

A Case of Strangulated Hernia with Volvulus.—HUGHES (*British Med. Jour.*, October 25, 1919, p. 527) reports a case which is interesting for several reasons: Volvulus occurring in a hernial sac is rare; the symptoms were remarkably mild considering the condition which existed; the patient gave no trouble during convalescence and the wound healed by primary intention despite the offensive nature of the sac contents. The hernia was a left-sided inguinal, which had been present for some months. The strangulation began the day previous. The omentum and bowel in the sac were gangrenous. It was found that the bowel was twisted on itself and that a true volvulus existed. The gangrenous omentum was removed and the gangrenous bowel resected, end-to-end anastomosis being done. The bowel dealt with was the pelvic colon. The patient made an uninterrupted recovery.

Radium in the Treatment of Tuberculous Adenitis.—MOLYNEUX (*British Med. Jour.*, November 29, 1919, p. 705) says that he is convinced that the day of radical operation for tuberculous glands will soon be past. Radium is, if properly used, a safe and, as far as he can see, a certain cure, whether for an early or an advanced case of tuberculous glands. He has treated between twenty and thirty cases during 1913-1914. Unless there were sinuses already present no scars were left. In no case was any ulceration caused. Fifteen milligrams of radium bromide applied on a special applicator for 150 mg. hours is suitable for each group attacked. The patients usually had two applications a week. The treatment is continued until all signs of trouble have disappeared. Three cases illustrating different degrees of the disease which were treated are reported.

The Importance of the Spleen in Resistance to Infection.—MORRIS and BULLOCK (*Ann. Surg.*, 1919, lxx, 513) says that very little experimental evidence to refute or support the widespread impression that the spleen plays a part in resistance to infection has been offered. No experimental work can be entirely trustworthy which does not include the recognition and elimination of outside sources of error. The work of Bardack, Roger, Tizzoni and Cattini, Kourlow and others is reviewed, showing the conflicting opinions on the question. On the whole it cannot be said that the blood changes following splenectomy furnish any positive evidence of an impaired ability on the part of the body to

resist infection, but they may be an indication of increased susceptibility to infection and imperfect reaction against it. Thirty-six splenectomized rats were used together with thirty-six controls. It was observed that the splenectomized animals almost invariably died before the controls when they were exposed to chance laboratory contagion, the death-rate among the splenectomized animals being 80.5 per cent. as compared to 38.9 per cent. in the controls. Their results after numerous carefully controlled experiments show in a very definite manner that while the animals get along fairly well without a spleen in the absence of any infection, the reverse is the case when the organism is put to the strain of resisting acute bacterial invasion. Under the circumstances they infer that the spleen normally aids tremendously in resisting infectious processes in rats, and that its removal temporarily robs the body of its resistance until such a time, at least, as compensatory processes will have a chance to reestablish this.

THERAPEUTICS

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UNDER THE CHARGE OF

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Arterial Hypertension.—ALLEN (*Jour. Am. Med. Assn.*, 1920, lxxiv, 652) deals in this article particularly with the restriction of salt and fluid as therapeutic agents in the treatment of hypertension. He believes that suitable chloride restriction is a great factor in making patients with hypertension more comfortable, diminishing the danger of apoplexy and possibly checking the progressiveness of the disorder. By far the best results are obtained in the earliest cases when the hypertension is intermittent rather than continuous. Early diagnosis, therefore, is important, and Allen hopes that chemical tests, such as for blood chlorides and chloride threshold (the normal values of which are still undecided), may help in the early diagnosis. The practical application of low chloride and diminished fluid intake has certain limitations, which he mentions: (1) A diet reasonably satisfying, and at the same time poor in salt, is a difficult diet to arrange. (2) A certain quantity of salt is considered indispensable in a permanent ration. This is stated as approximately 2 gm. for normal individuals. The limits have not been determined for nephritis patients. The chief untoward effect of salt deprivation is weakness, and it is therefore necessary to work out salt rations for individual nephritic patients. (3) Such restriction of salt or fluid is only palliative, and success is not as universal as, for instance, in the treatment of diabetes.

The Role of Carbohydrates in the Treatment of Toxemia of Early Pregnancy.—TITUS, HOFFMANN and GIVENS (*Jour. Am. Med. Assn.*, 1920, lxxiv, 777) discuss the subject of the treatment of the toxemias of pregnancy. They are convinced, from their clinical experience, that liberal carbohydrate feeding is beneficial in the treatment of this disturbance. Mild cases of nausea and vomiting may be controlled by increasing the carbohydrates of the diet and an avoidance of more than short intervals of fasting by the taking of food more frequently. Increased carbohydrate intake is obtained by giving the patient from 8 to 16 ounces of a 10 per cent. glucose and 2 per cent. sodium bicarbonate solution daily by mouth. More severe cases may require increased quantities of this solution, given both by mouth and by rectum. They give to seriously toxic patients additional carbohydrate, easily utilizable, by intravenous injection of from 15 to 25 gm. of glucose in from 250 to 300 c.c. of water. This is given from one to three times daily. They believe that the intravenous injection of glucose solution is a valuable therapeutic measure, and also that the rate of its absorption and storage by the liver is an index of liver efficiency that is of prognostic value.

Protein Diets and Undernutrition in the Treatment of Diabetes.—ALLEN (*Jour. Am. Med. Assn.*, 1920, lxxiv, 571) states that a possible diet after fasting is one composed wholly or chiefly of protein, and this plan has seemed the most useful for maintaining strength during the period of undernutrition necessary for attaining a normal blood-sugar. Actual suffering from hunger is prevented by the use of materials to furnish bulk (bran, agar, cellulflour, "India gum," liquid petrolatum, soups, small quantities of thrice-boiled vegetables), without which such low diets would scarcely be practicable. In some elderly patients slight hyperglycemia and nitroprusside reactions may be permissible to avoid undue hardships, but diabetes after the age of forty is by no means always benign, and not infrequently requires stringent measures to control it, especially after long neglect. The more severe the diabetes and the younger the patient the more rigorously should hyperglycemia and all other symptoms be controlled from the outset. Such a policy often means a considerable reduction of weight and strength as compared with the level which can be maintained temporarily by higher diets, and its justification depends on the belief that patients are best off in the long run when their weakened function is spared as thoroughly as possible.

Treatment of Bronchial Asthma.—GOTTLIEB (*Jour. Am. Med. Assn.*, 1920, lxxiv, 931) discusses the treatment of bronchial asthma from its various standpoints, climatic, specific and drug. He believes that the climatic treatment is only of value in cases of asthma due to anaphylaxis to various pollens and that the beneficial effect is due to removal of the exciting cause. Patients who are anaphylactic to foods are benefited by the elimination of such articles from their diet. Those patients who are sensitive to bacterial proteins alone, or, as frequently occurs, complicated by food anaphylaxis, frequently receive benefit from bacterial vaccines. In case the vaccine treatment subcutaneously has no effect, intravenous injections should be tried. Great care is necessary in the

administration of the proper dose. The author is of the opinion that in about 50 per cent. of the cases of hay-fever asthma the attack can be controlled by prophylactic and specific treatment. It is essential that the degree of sensitiveness be determined before administering the treatment. This may be done by testing the patient with varying dilutions of the pollen extract. He considers that it is better to give the treatment throughout the year rather than a short period of treatment during the hay-fever season. Regarding drug therapy, the author speaks of the beneficial effect of epinephrin given hypodermically in dilutions of 1 to 1000 in controlling the acute attack of dyspnea. The effects generally last for from one-half to two hours. As a rule, patients gradually become accustomed to repeated doses of epinephrin, so that the amount given has to be increased from time to time, and finally often a complete tolerance to the drug is developed and no relief is obtained from its administration. Atropin given subcutaneously or intramuscularly in gradually increasing doses up to the point of tolerance will frequently give relief. KI by mouth is frequently of distinct value. The inhalation of fumes of burning stramonium leaves and potassium nitrite gives relief in acute paroxysms.

PEDIATRICS

UNDER THE CHARGE OF

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A Case of Hypersensitiveness to Cows' Milk.—PARK (*Am. Jour. Dis. Children*, January, 1920), reports a case of a child who is now three years old. At six weeks it was given a supplementary feeding of a cow's milk formula once a day. It took about one ounce, amounting to about 10 c.c. of cow's milk. It fell asleep and when aroused it vomited. It was very pale and heavy. It refused the next breast nursing, and vomited again, after which it fell into a heavy sleep. It took the next breast feeding and the next day it seemed normal. Thinking that the baby was hypersensitive to cow's milk it was given a teaspoonful of a mixture of milk diluted one-half with water. After taking this it was nursed and immediately fell asleep. It occasionally opened its eyes and yawned. The face became flushed. About five hours after taking the mixture it vomited in small amount, and ten minutes later it vomited a large amount of bile-stained fluid. It became exceedingly pale and seemed greatly prostrated. Shortly after vomiting it had two large loose stools containing mucus. It refused the next nursing, and slept heavily until the next nursing period when it nursed in a normal manner. After cutaneous test there were delayed general reactions locally, the tests were negative. It was able to take goat's milk without any difficulty. Intracutaneous tests of various proteins were done and gave slight local and delayed general reactions. There was a

marked but delayed local reaction to cow's milk. The same general effects followed the accidental administration of a condensed milk mixture. An attempt was made to desensitize the baby, and after some time and with perseverance this was accomplished. He is now able at three years to take a pint of cow's milk daily without any difficulty. At eight months of age it was necessary to wean him from the breast, and it was necessary to feed him on goat's milk, which singularly enough gave rise to no reaction. From the evidence of the case the author considers this peculiarity as having been inherent in the germ plasm.

Dextrose Tolerance in Atrophic Infants.—MATTILL, MAYER and SEINER (*Am. Jour. Dis. Children*, January, 1920) remind us that by the Woodyatt method it has been shown that the tolerance of adults was from 0.8 to 0.9 grams per kilogram per hour. In this study they gave dextrose solutions intravenously to four non-atrophic infants, ranging in age from five to fifteen months. In these cases the tolerance was found to be 0.8 to 0.9 gram per kilogram of body weight per hour. Seven atrophic infants were studied. They showed emaciation, tendency to subnormal temperature, lack of turgor and grayish color of the skin. Their weights were stationary or nearly so. The stools were good. In no case was tolerance below 1.4 or 1.5 gram, per kilogram of body weight per hour. Other authors have also found that the metabolism of the atrophic infant proceeded to a higher level than that of the normal infant. McClure and Sauer have observed that atrophic infants have a higher surface temperature than normal infants and there is an increased insensible perspiration. An increased sugar tolerance seems to fit in very well with such observations. It was observed that the readings were constant in the cases in which several injections were given.

Mental Defectives in a Southern State.—ANDERSON (*Mental Hygiene*, October, 1919) gives a report of the Georgia Commission on Feeble-mindedness and the survey of the National Committee for Mental Hygiene. As a result of this survey he says that 40 per cent. of the inmates of the almshouses were feeble-minded. Feeble-minded families had been found in the State that had been supported by church and organized charities for three or four generations. A study of a typical orphanage showed that 28.7 per cent. of the children were feeble-minded. If the same percentage exists in the other orphanages in the State, there are at least 810 feeble-minded in orphanages who need special care and training in a school for the feeble-minded. At the state prison farm 17.5 per cent. of the inmates were feeble-minded. The striking fact at this institution was not so much the presence of feeble-minded men, but the great number of other forms of mental abnormality, mental disease and deterioration, epilepsy and the like. In this institution 65.8 per cent. of the inmates were classifiable in terms of deviation from normal mental health. Of the women inmates of the prison 42.8 per cent. were found to be feeble-minded. In the two typical county jails studied 34 per cent. of the inmates were feeble-minded, with a mental level of ten years or under. Of 122 immoral women examined 43.5 per cent. were found to be feeble-minded. The

present policy of treating these feeble-minded girls for venereal disease and then turning them into the community to acquire it over again is costly. Probably the greatest factor in the spread of venereal disease is the feeble-minded prostitute. Of 100 cases of juvenile delinquents studied in the juvenile courts, 17 per cent. were found to be feeble-minded, In one reformatory for boys, 15 per cent. were feeble-minded. In the State Reformatory for boys 24.1 per cent. were feeble-minded and in the State Training School for Girls 27 per cent. of the inmates were feeble-minded. These feeble-minded delinquent children later become the chronic habitués of the jails, courts and prisons. In the public schools 3.5 per cent. of the children examined were feeble-minded.

Control of Diphtheria by Cultures of the Noses and Throats of School Children.—GLOYNE (*Jour. Am. Med. Assn.*, January 10, 1920) gives the results obtained in Kansas City, of which he is Health Commissioner. He says that the swabbing of the throats of the children should be a measure adopted at the outbreak of a single case of diphtheria in a school. The quarantine of carriers is as essential as is the quarantine of those suffering from diphtheria. Two negative cultures should be required as the minimum from all children who have had a positive culture. A negative culture means something, but it does not have the significance that a positive culture has. Antitoxin has a very definite place in giving immunity against diphtheria, but it does not kill the diphtheria bacillus. For this reason those who have had diphtheria may continue to be carriers for an indefinite time if great care is not taken to get at least two negative cultures. Carriers usually clear up in time without the use of antitoxin.

Methods of Administering Saline and Other Solutions to Infants and Children.—AIKMAN (*Jour. Am. Med. Assn.*, January 24, 1920) says that the administering of physiologic sodium chlorid and other solutions to replace fluids lost from the body is a valuable method of carrying certain cases over critical periods. Loss of fluid is often a more serious condition in children because of the vomiting that so often accompanies grave illness, and because of the difficulty of giving water by mouth. A relative acidosis may easily result, which in a few hours may greatly increase the gravity of the attack. The reduction of fluid is more marked in cases with a history of numerous watery stools characterized by a rapid loss of weight, hollow eyes, and drawn, pinched expression of the facies. The method of greatest service is that which will permit the introduction and retention of large amounts of fluid with the greatest ease to the operator and with the least discomfort and danger to the patient. The methods used are: Administration by mouth; rectal administration; hypodermoclysis; intravenous injection by the intrasinus method or by injection into the femoral vein; intra-peritoneal injection. The author has done considerable work with this method and describes it in detail as follows: The instruments needed are a medium-sized intravenous needle, an infusion bottle and rubber tubing. The skin of the abdomen is carefully sterilized with tincture of iodine and alcohol. The skin and the subcutaneous tissue are picked up between the thumb and the forefinger, and the needle is introduced in an upward direction through the abdominal wall in the midline just below the umbilicus. Care must be taken to avoid piercing

a distended bladder, and while there is also danger of puncturing the intestine, no record of this accident has been encountered. In cases in which necropsy was performed there was found a small hemorrhagic area in the abdominal wall and peritoneum, but no injury of serious importance. When the needle has passed into the abdominal cavity, the solution is introduced by gravity. It was found much easier to use the infusion bottle. Warm physiologic sodium chlorid solution has always been used, of which from 100 to 250 c.c. may be given every twelve to twenty-four hours. In older children 300 to 400 c.c. may be given and if no untoward signs develop it may be given until the abdomen is slightly distended. The injection must always be made slowly. After the operation the abdomen should be covered with a sterile dressing. It has been shown by the phenolsulphonephthalein test and by necropsy that from 40 to 60 per cent. of the fluid is absorbed in one hour. The remaining solution acts as a reserve, the gradual absorption of which explains the more protracted improvement in this method as compared to the results obtained by other methods.

Vomiting in Infants.—MARFAN (*Le Nourrison*, March, 1919) describes the vomiting of nursing children as a disease of habitual vomiting in nursing. The gastric mucous membrane is unduly sensitive and after each feeding there is a gastrospasm and the stomach casts up more or less of its contents. It is a gastric neurosis and this explains the variability of the findings in the chemistry of the stomach and of the stools. If the spasms include the bowel there is constipation. In some cases there is excessive swallowing of air. These children all show some neuropathic tendency. As regards the treatment, in some cases the treatment for inherited syphilis gives surprisingly good results. Sometimes a complete change of environment is necessary. The matter vomited in these conditions is usually a colorless fluid made up of whey, swallowed saliva and gastric juice, with floating clots of milk, as the vomiting does not occur immediately after taking food, but from fifteen minutes to one and a half hours after feeding. The vomiting may occur without effort or the child may be restless and scream and appear relieved after vomiting. Sometimes abruptly moving the child will bring on the vomiting.

GYNECOLOGY

UNDER THE CHARGE OF

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Conservative Myoma Operations.—The question of the advisability of performing myomectomy rather than hysterectomy in certain cases

of uterine myomata has been discussed on numerous occasions but as yet there is anything but unanimity on this point among gynecologists. The question has recently been investigated in the Frauenklinik at Lund by ESSEN-MOELLER (*Monats. f. Geb. u. Gyn.*, 1919, 1, 36) from five different standpoints, namely the immediate operative results, ultimate results, recurrences, subsequent labors and malignant degeneration of the myomata or of the remaining uterus. Concerning the first question, in spite of the fact that for many years myomectomy has always been considered to have a higher mortality than hysterectomy, the author quotes statistics from European as well as American sources to show that such is not the case, while he personally has performed 34 myomectomies without a death. He is therefore of the opinion that the conservative myomectomy offers practically as good a primary result as hysterectomy and therefore the latter operation should be confined to those cases which are technically very difficult or in which there is malignant degeneration of the growth. Taking up the question of the ultimate results of operations he states that 80 per cent. of the cases that have had hysterectomies performed for myomata have been relieved of their symptoms while only 40 per cent. of the myomectomy cases have been so relieved since many of these latter cases continue to suffer from bleeding and annoying discharges. Therefore from this standpoint hysterectomy would be the preferable operation. Concerning the question of recurrence of myomata after the conservative operation, much will depend on the number of years elapsing between the operation and the examination, because the greater the lapse of time, the larger will be the number of cases in which a recurrence will be found. The mere fact that another myoma has grown, however, is not an indication for a second operation as many myomata give no symptoms or other inconvenience. Of the 21 patients that this author examined after myomectomy there was a recurrence in 7 but of these a second operation was necessary in only four patients. Nevertheless there can be no question but that myomectomy is distinctly inferior to the radical operation from the standpoint of recurrence. When we consider the possibility of a subsequent pregnancy after operation, there is no comparison between the two operations. Indeed it is this one point that stands as the chief argument in favor of the conservative operation since pregnancy is impossible after hysterectomy. The number of pregnancies that occur after myomectomy is doubtful, the reports of various operators giving statistics varying from 72 per cent. to 3 per cent. A close study of the literature seems to show that the possibility of subsequent pregnancy is most likely when the patient is under forty years of age and also when the tumor that was removed was of a moderate size. Large or multiple growths reduce the possibility of later gestation. In regard to the possibility of subsequent degeneration of the uterus that is left behind, the author has little to say since the pathologists themselves cannot always agree as to whether or not a given picture is malignant. The gynecologist must perform the radical operation in all cases in which there is a suspicion of malignant degeneration, which cases are usually patients over forty years of age in whom myomectomy is not the operation of choice from any standpoint.

Radium Treatment of Cervical Cancer.—KELLY and NEILL (*Am. Jour. Surg.*, 1920, xxxiii, 289) give a brief historical sketch of the use of radium in the treatment of cancer, stating that when radium was first used, and it was found that big cancers of the cervix melted down so remarkably under direct applications at the vaginal vault, a number of surgeons soon ran out before the world, waving their arms frantically like Archimedes of old and shouting, "Eureka! No more surgery; radium cures all these cases; the panacea for cancer is found at last." But the sad experience of many recurring cases began in a couple of years' time to dampen even the ardor of these neophytes, until at last a soberer judgment reigns. The present status of the case seems to be this: In early and very favorable operative cases, operation, preceded by thorough radiation, offers the best chance. Yet even here Kelly concedes that if the patient is near enough to the radium therapist to be seen at intervals, and will conscientiously keep under observation, radium alone will probably do more than operation and without risk of mutilation. He ventures to predict that within five years we are all of us likely to be using radium to the utter exclusion of operations. In all other cases, except this group, most favorable for surgery, that is to say, in all in which there is any lateral fixation of infiltration of the parametria, radium will do more for the patient than operation, for here recurrences are almost invariable. In some of these cases, as in masses of disease elsewhere, lingering nodules can often best be treated by the insertion of the minute capillary sealed glass points, each containing from three to five millicuries of emanation right into the tissues by means of a specially constructed hypodermic needle. The points are buried and lie innocuous in the tissues and the emanation sinks to zero in about five days. The authors conclude that in radium therapy, as in surgical therapy, two things are of vital importance: (1) That the earlier that the case is seen the better are the chances of a permanent result; (2) that every case ought to be followed up carefully at intervals of a few weeks or months for years. They believe that the best work in the treatment of cervical cancer will be done by the man who commands both resources and can resort with equal facility either to radium or to surgery, or can employ both conjointly as seems best.

Roentgen Treatment of Benign Bleeding.—In the treatment of the various types of uterine bleeding due to a benign cause by means of the roentgen ray, MEYER (*New York Med. Jour.*, 1920, cxi, 143) states that in a single treatment of from forty to ninety minutes' duration, depending upon the size of the patient, a permanent cessation of the menstrual function and of hemorrhage can be produced. In his last series of twenty consecutive cases, in which doses based on absorption percentage administered at a single sitting were employed, the ages ranged from seventeen to forty-five years, with no failure in the series. The symptoms of the menopause are materially diminished and the period of suffering shortened by one or two applications. The contraction of larger fibroids may require three or more repetitions of

the treatment. When more than one treatment is to be given, from four to six weeks should elapse between applications, not alone to await full reaction, but to allow the skin to recover from the cumulative effect of the rays. The fibroid growths best suited to irradiation are the intramural type. The subperitoneal and particularly the pedunculated variety had best be removed surgically according to Meyer. The submucous or polypoid type of fibroids are practically contra-indications to the use of radiotherapy. When complications, and above all malignancy do not exist, the results are uniformly good. A careful examination and correct diagnosis are essential or the result may be anything but pleasant.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Non-Lactose Fermenting Organisms from the Feces of Influenza Patients.—Stimulated by the occurrence of intestinal manifestations of influenza in the recent pandemic SHERWOOD, DOWNS and McNAUGHT (*Jour. Infect. Dis.*, 1920, xxvi, 16) undertook bacteriological examination of feces of cases of this particular type. Eosin-methylene blue agar plates and Russell's medium were used for growing cultures from feces and following isolation, strains were grown on the various sugar and alcohol media. Enteriditis-like organisms were isolated from a high percentage of influenza cases of above-mentioned type. By means of agglutination and absorption tests (modified Dryer technic) strains of enteriditis like organisms were apparently placed in four groups. B. typhosus was isolated from three of 32 cases studied. There seemed to be no correlation between the nature of the stools and the presence of the enteriditis-like bacilli.

Hemolytic Streptococci in the Throat in Certain Acute Infectious Diseases.—OTTERAAEN (*Jour. Infect Dis.*, 1920, xxvi, 23) reports the relative occurrence of hemolytic streptococci in the throats of 300 patients. Swabs taken from mouth, nose and throat were cultured on blood agar plates. Fermentation tests of 50 strains gave results showing that according to Holman's classification the strains fell into the pyogenes and anginosus groups. Fifty-eight of 130 diphtheria cases and 98 of 125 scarlet fever cases gave positive streptococcus cultures. Results show that the throat is the area of predilection, while the nose and mouth do not seem to harbor the organisms frequently. The great majority of these patients were children, most of whom had more or less enlarged tonsils. Virulence for animals of the organisms studied was low. Human leukocytes, in the presence of normal human serum, easily phagocyted the hemolytic streptococci which had been

cultivated on media for a time. Other hemolytic streptococci isolated from lesions in the body where they demonstrated invasive qualities were not phagocyted until grown on artificial media, which seems to show that resistance of hemolytic streptococci to opsonins may be lost rapidly in artificial cultivation. After a comparative study the author suggests the enrichment method as preferable to direct surface plate inoculations in examinations for streptococci.

Further Attempts to Reduce the Resistance of the Guinea-pig to Tuberculosis.—Attempts were made by CORPER (*Am. Rev. Tuberc.*, 1919, iii, 605) to reduce the resistance of experimental animals to the tubercle bacilli with a view of hastening the animal diagnosis of tuberculosis. The experiments also offered an interesting study on tissue resistance when injured. A variety of methods have been advocated by various authors, for the early diagnosis of tuberculosis by injecting suspected material into different regions where tissue damage had been induced. The author studied the effect of trauma, mechanically induced or resulting from chemical irritants. Glands were crushed; lampblack or powdered glass were injected; or chemical irritants as turpentine, croton oil, cantharidin, and capsicum were injected. In the region of the injury small amounts of tubercle bacilli were inoculated, using the macroscopic-anatomic tuberculosis as an index of the acceleration of the tuberculosis in the guinea-pig. It was found that gland crushing, the injection of turpentine, croton oil, cantharidin and capsicum just prior to injection of virulent tubercle bacilli had no appreciable effect upon the infection as compared with that obtained in control guinea-pigs. Lampblack simultaneously injected with tubercle bacilli had a retarding influence while powdered glass enhanced the development of the lesions.

A Strain of Connective Tissue Seven Years Old.—An interesting report of a strain of connective tissue isolated in January, 1912, and cultivated for a period of seven years is given by EBELING (*Jour. Exper. Med.*, 1919, xxx, 531). Transfers of portions of the tissue were made each forty-eight hours into a medium composed of equal volumes of chicken plasma and chick embryo extract, under the usual aseptic precautions. These transfers were incubated at 39° C. on coverslips sealed by vaseline and paraffine, to hollow glass slides. The growth of the transferred tissue was measured by means of a projection apparatus. The rate of growth was such that transplanted fragments became 13 times their original size in forty-eight hours. The rate varied, however, up to as high as 40 times the original size, under the influence of various factors. There was noted an evident increase in the rate of growth in the last five years, thought due to the addition of the embryonic juice to the medium. It was always found that decrease in rate of growth was due to deficient medium or extract, or the presence of alkali at the surface of the slides. Plates are shown.

Streptolysin Production in Carbohydrate Media.—STEVENS and KOSER (*Jour. Exper. Med.*, 1919, xxx, 539) present a study of various factors influencing the development of hemolysins in cultures of streptococci. A review of previous work is given. Theories of acid inhibi-

tion of growth of streptococci with subsequent diminution in hemolysin, as well as the sparing of protein metabolism (through which lysin is elaborated in the bacterial body) in the presence of fermentable carbohydrates thus diminishing lysin production. By incubating cultures of streptococci in beef infusion, peptone, serum broth for ten to fourteen hours and passing through Mandler filters they were able to obtain strongly hemolytic filtrates. Acid production in carbohydrate was followed by comparison to Sorensen series. The growth of the streptococci was followed by plate counts and stained smears. The utilization of carbohydrates by the streptococci, thus producing a luxuriant growth is at the same time accompanied by a lessened lysin production through the sparing of the proteus. The acid production reaching a value of pH 5.5 in eight hours in dextrose media, lessened the vitality of the organisms and thereby proteolysis, and is found to be destructive to hemolysin at incubator temperature. The concentration of the acid produced causes some hemolysis and a coincident brown discoloration of the hemoglobin.

The Bacteriology of Chronic Empyema.—In the past few years the bacteriology of empyema as seen in civil and especially military practice has presented several predominating types of organisms, as principal etiological factors. GORDON (*Jour. Infect. Dis.*, 1920, xxvi, 29) presents a study of the relative occurrence of these organisms and of other bacteria in empyema. The pneumococcus and streptococcus were found to be the principal primary invaders. Secondary post-thoracotomy infection, which is the rule, introduces a number of other bacteria which vary in character and quantity, as the case develops chronicity. Cultures were made on blood, beef infusion agar, from materials obtained by aspiration of pus pockets by syringe before operation, and from a looped needle introduced through a sterile tube inserted through the drainage opening, at weekly intervals. Subsequently for three months type II pneumococcus was found in one of 25 military cases, and in the other 24 hemolytic streptococci were the primary invaders. Green streptococci, *Staphylococcus albus* and *aureus*, diphtheroids and chromogenic air bacteria were found as secondary infecting agents. However, two proteolytic bacilli, one an atypical member of the proteus group, the other an atypical member of the Friedländer group were found to be the most common secondary invaders. The cultural and biological characters of these two are given. Agglutinins in the sera of 20 of 25 patients, titred from 1 : 400 to 1 : 3200 against a representative streptococcus pyogenes (Holman's classification) isolated from the chest fluid. The absence of streptococci in culture from empyema fluids at the time the serum was obtained would indicate an active immunity against those organisms. No agglutinins could be demonstrated against various streptococcus viridans strains isolated from a number of cases. Controls of serum from normal cases were negative.

Serum Reactions in Influenza.—Following their investigation of the etiology of influenza, in the recent epidemic, GAY and HARRIS (*Jour. Infect. Dis.*, 1919, xxv, 414) present results of work on rabbit immune serum, the serum of active and recovered influenza cases, and of persons vaccinated by the injection of a presumably protective dose

of a mixed vaccine comprising 18 strains of influenza bacilli. Rabbits were immunized by six to eight injections of a mixed vaccine of ten strains of *Bacillus influenzae* grown on "chocolate medium," and killed by suspension in 0.5 per cent. phenolized salt solution. After a first injection of killed organisms, living cultures were employed. Agglutination tests at 37° C. for two hours, with the serum of immunized rabbits, also Pfeiffer's phenomena of bacteriolysis, conglutination and precipitin reactions were negative. Fixation antibodies were found in high dilutions. Agglutination tests with the same serum, incubating three to six hours at 55° C. were positive. A variation in the agglutinability of different strains of *Bacillus influenzae* suggests the existence of different groups of the organism. In the series of human cases, agglutination tests at 37° C., conglutination, opsonin, precipitin, and intradermic tests were negative. Fixation reactions were positive in 40 per cent. of vaccinated cases and in one of twenty-nine acute cases; normal and recovered cases were negative. Agglutination tests at 55° C. were positive in from three to six hours in 88 per cent. of acute cases, 46 per cent. of vaccinated and 38 per cent. of recovered cases. The few normal cases tested were uniformly negative.

HYGIENE AND PUBLIC HEALTH

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Experiments on the Nasal Route of Infection in Poliomyelitis.—FLEXNER and AMOSS (*Jour. Exp. Med.*, 1920, xxxi, 123) state that the experiments given in their paper, notwithstanding their seeming diversity, relate to the conditions underlying the states of susceptibility and refractoriness to infection with the virus of poliomyelitis applied to the nasal mucosa. Certain monkeys are highly refractory to inoculation *via* the nares, with the virus of poliomyelitis, apparently in virtue of a power possessed by the nasal mucous membrane to destroy or otherwise render ineffective the virus applied to it. This property of the nasal mucosa appears to be distinct from any specific protective substance active upon the virus which may occur in the blood. An effective nasal mucous membrane prevents the passage of the energetically applied virus to the brain and spinal cord. The virus of poliomyelitis energetically applied to the nasal mucosa will survive for an undetermined period of time upon an ineffective, but for a relatively brief period of time upon an effective membrane. The

protective power possessed by the nasal mucosa is not in itself adequate to prevent infection with the virus introduced upon it, since slight injury to such independent structures as the meningeal-choroid plexus complex favors the passage of the virus from the nose to the central nervous organs. The normal nasal mucosa is, therefore, an invaluable defence against infection with the virus of poliomyelitis; and the number of healthy and chronic carriers of the virus is probably determined and kept down through the protective activities of this membrane. Antiseptic chemicals applied to the nasal mucosa upon which the virus has been deposited exhibit no great protective action and are of doubtful value. Indeed, it is not impossible that to the extent to which they may affect unfavorably the destructive properties of the nasal mucosa they may be even objectionable. Infection with the virus of poliomyelitis applied to the nasal mucosa under conditions favorable to the extension to the central nervous organs and multiplication there may be blocked or prevented by the injection of poliomyelitic immune serum into the blood. While the exact manner and site of attack of the immune serum upon the virus is somewhat conjectural, when all the available data are considered it seems probable that the meeting-place of the virus and immune serum is in the subarachnoid space.

The Physical and Economic Benefits of Treatment for Hookworm Disease.—SCHAPIRO (*Jour. Am. Med. Assn.*, 1919, lxxxiii, 1507) states that although the life, labor and customs of the people living on the two estates studied do not differ from those that obtain generally throughout the country (Colombia), and although every effort was exercised to guard against error in conducting the study, the number of cases studied is probably insufficient to justify the drawing of conclusions that will apply to whole territories. Nevertheless, the figures may be taken as pointing toward, if not as establishing the following: There is a permanent increase in hemoglobin as a result of treatment for hookworm disease. On one farm in spite of a 15 per cent. reduction in unit pay the laborers earn 27 per cent. more. On another, where there has been no reduction in unit pay, they earn 14.6 per cent. more. The owners of one farm are cultivating 33 per cent. more coffee with the same number of laborers at a lower unit cost. In addition to the benefits mentioned one estate reports a marked reduction in morbidity and in infant mortality, and both estates report that the laborers spend less than formerly, or else spend nothing at all, for quack medicines and quack physicians to cure their infirmities.

The Chemotherapeutics of the Chaulmoogric Acid Series and Other Fatty Acids in Leprosy and Tuberculosis.—WALKER and SWEENEY (*Jour. Infect. Dis.*, 1920, xxvi, 238) state that chaulmoogra oil contains bactericidal substances that are about one hundred times more active than phenol. The bactericidally active substances of chaulmoogra oil are the fatty acids of the chaulmoogric series, chaulmoogric and hydrocarpic acids and possibly lower isomers of this series. The bactericidal activity of the chaulmoogric acid series is specific for the acid-fast group of bacteria and inactive against all other bacteria tested. This specific bactericidal activity against acid-fast bacteria is a function of the carbon ring structure of the molecule of the

chaulmoogric acid series, which, so far as known, is found only in chaulmoogra oil and in oils of certain plants closely related to *Taraktogenon kurzii*. The fatty acids of cod-liver oil, the salts of which constitute Roger's sodium morrhuate, used in the specific treatment of tuberculosis, do not possess the specific bactericidal activity of the chaulmoogric acid series. These facts supply a scientific basis for the use of chaulmoogra oil and its products in leprosy. Their experiments do not support the claims of Rogers for sodium morrhuate in the specific therapy of tuberculosis. The bactericidal activity of the chaulmoogric acids against all members of the acid-fast group of bacilli, together with the clinical results obtained from their use in leprosy, furnish theoretical grounds for the application of the chaulmoogrates to the therapy of tuberculosis. Experiments on animals are now in progress to determine whether or not the chaulmoogric acid series have any practical value in the chemotherapy of tuberculosis.

An Experimental Study of the Efficacy of Gauze Face Masks.—KELLOGG and MACMILLAN (*Am. Jour. Public Health*, 1920, x, 34) state that gauze masks exercise a certain amount of restraining influence on the number of bacteria-laden droplets possible of inhalation. This influence is modified by the number of layers and fineness of mesh of the gauze. When a sufficient degree of density in the mask is used to exercise a useful filtering influence, breathing is difficult and leakage takes place around the edge of the mask. This leakage around the edges of the mask and the forcible aspiration of droplet-laden air through the mask is sufficient to make the possible reduction in dosage of infection not more than 50 per cent. effective. It remains for future controlled experiments on contagious disease hospitals to determine whether the wearing of masks of such texture as to be reasonably comfortable are effective in diminishing the incidence of infection. Masks have not been demonstrated to have a degree of efficiency that would warrant their compulsory application for the checking of epidemics.

Causes of Blindness. The National Committee for the Prevention of Blindness has tabulated the statistics of schools and day classes for the blind for October, 1919. Among these, out of a total of 3847; 879, or 22.8 per cent., were caused by ophthalmia neonatorum. Some of the other causes of blindness in the above total are: Blind from accident, 304; progressive nearsightedness, 80; trachoma, 53; interstitial keratitis, 178; optic nerve atrophy, 394; congenital cataract, 411; and other congenital causes, 556.

The Eye as a Portal of Infection in Respiratory Diseases.—CORPER and ENRIGHT (*Jour. Am. Med. Assn.*, 1920, lxxiv, 521) state that the eye must be considered as one of the important portals of infection in respiratory diseases, and, although the greater part of the infectious material entering by way of the eye is subsequently swallowed and passes into the gastro-intestinal tract, a small but definite portion of it finds its way into the larynx and trachea, where it may persist even as long as a week. In its passage from the eyes the infectious material traverses a definite channel, dependent on which eye it has

entered or into which it has been introduced. Infectious material that is ingested is far less likely to enter the respiratory tract than that entering by way of the eye or nose.

Studies on Preservatives of Biological Products.—NEILL (*Hygienic Laboratory Bulletin No. 112*, U. S. Public Health Service, Washington, D. C.) studied the effects of widely employed preservatives on contaminations accidentally found in biological products. He found that certain contaminating organisms were extraordinarily resistant to the killing action of phenols and of formaldehyde, though resistance to one preservative did not necessarily correspond to resistance to another. Some organisms were not killed by the maximum concentrations that may be safely used in biological products. The necessity for scrupulous care in the preparation of the products is emphasized.

Immunization Against Typhus Fever.—While the clinical evidence of successful transmission of typhus infection to laboratory animals is not very striking, yet when it is supported by properly conducted controls, it is trustworthy. By those who have had extensive experience with experimental typhus, the appearance of fever in the rhesus monkey ten days after inoculation of virulent typhus blood, and its continuance for ten days are accepted as postulates of successful infection. Since the classic cross-immunity experiments of Anderson and Goldberger conclusively demonstrated the identity of the causal agents of Mexican typhus and Brill's disease, and consequently the identity of the two, it follows that any claim for the successful isolation of the causal agent of Typhus exanthematicus would be best established on the basis of the production of experimental typhus and cross-immunity with virulent typhus blood. McCoy and NEILL (*Public Health Rep.*, June 1, 1917), in carefully controlled experiments, report complete failure with the inoculation of living and killed (60° C.) cultures of *B. typhi exanthematici* (Plotz) to produce either experimental infection in the rhesus monkey, or any evidence of immunity against inoculation with virulent typhus blood. They conclude merely that they have presented evidence that a bacterial vaccine prepared from *B. typhi exanthematici* (Plotz) failed to protect monkeys against Mexican typhus.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1913 Spruce St., Philadelphia, Pa., U. S. A.

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